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Knüppel, Ane

Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

OUTCOMES FOR ADOLESCENTS AND YOUNG ADULTS DIAGNOSED WITH AUTISM SPECTRUM DISORDER IN CHILDHOOD

BY
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DISSERTATION SUBMITTED 2018

AALBORG UNIVERSITY
DENMARK

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Dissertation submitted 2018

Dissertation submitted: January, 2018

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PhD Series: Faculty of Medicine, Aalborg University

Department: Department of Clinical Medicine

ISSN (online): 2246-1302
ISBN (online): 978-87-7210-143-9

Published by:
Aalborg University Press
Langagervej 2
DK – 9220 Aalborg Ø
Phone: +45 99407140
aauf@forlag.aau.dk
forlag.aau.dk

Printed in Denmark by Rosendahls, 2018

CV

I graduated from Aalborg University, Denmark in 2009 after finishing my master's degree in psychology. The interest in research emerged during my studies, continuing after graduation, and gave rise to my first job as a psychologist, where I worked as a research assistant on a project looking at language development in young children. Subsequently, I was employed as a clinical psychologist undertaking psychological assessment of preschool children with language impairments.

From 2010 to 2015 I was employed as a clinical psychologist at the Department of Child and Adolescent Psychiatry in Aalborg, and achieved authorization by the Danish Psychological Association in 2012. In 2015, I enrolled as a PhD student at Aalborg University Hospital, working in the Research Unit for Child and Adolescent Psychiatry. The topic of my PhD project is the outcomes of adolescents and adults diagnosed with autism spectrum disorder (ASD) in childhood. Additionally, I was involved in an international research project where the aim was to develop core sets of the International Classification of Functioning (ICF) for ASD and ADHD populations. This project was the basis for a stay abroad at the Karolinska Institutet, Sweden (2016). During the period of my PhD research, I have presented a poster at the International Meeting For Autism Research (IMFAR) in the USA (2017), and gave an oral presentation at the 16th Congress of the International Federation of Psychiatric Epidemiology in Australia (2017).

Ane Knüppel, January 2018

ENGLISH SUMMARY

The outcomes for children diagnosed with autism spectrum disorder (ASD) have been investigated for several decades. However, previous research is often characterized by relatively small and selected study samples as well as a normative focus when defining outcome. Yet, there is a growing focus on assessment of quality of life (QoL) in individuals with ASD, supplementing the normative defined outcome with a subjective perspective. It has repeatedly been found that the outcomes for the majority of adolescents and adults with ASD is poor, notwithstanding whether outcome is defined normatively as managing life independently or highly independently, or whether it is defined more subjectively in terms of QoL. Change in the concept of ASD over time complicates generalization of the results based on studies with samples diagnosed according to older diagnostic systems to newly diagnosed children with ASD. Additionally, the first cohort of children diagnosed with ICD-10 autism diagnoses is just about to reach adulthood. Accordingly, with the aim of supplementing and extending previous ASD outcome research, a nationwide survey with different estimates of outcome among adolescents and adults with ASD was conducted in this PhD project.

The study population was identified from the Danish Psychiatric Central Research Registry and was, together with parents, invited to participate in a survey about outcome, including adaptive functioning, QoL, and current daytime activity. The response rates for self-reports was 16.6% (n=933) and for parental reports it was 30.8% (n=1734), resulting in data for 1881 adolescents and adults with ASD with a mean age of 20.6 years, a mean age at diagnosis of ASD of 9.2 years, and a male:female ratio of 4.17:1. For the entire study population data from the national Danish registers were available allowing for analyses comparing responders and non-responders. Comparisons were made according to psychiatric history of the individuals with ASD, and sociodemographics of the individuals with ASD, as well as their parents, and only minor differences were found. However, there was a tendency that socioeconomically advantaged families more frequently completed the questionnaire. Overall, it can be assumed that the study population of adolescents and adults with ASD is, to a high extent, representative of individuals diagnosed with ICD-10 autism diagnoses in childhood.

Variability were found in the study population when described according to proportions of intellectual disability (ID), psychiatric comorbidity, and maladaptive behavior, as well as levels of adaptive functioning and autism symptoms. However, there was a tendency, compared with other studies, that lower proportions of behavioral problems and comorbidity were found, as well as higher levels of adaptive functioning, indicating that a subgroup of adolescents and adults with ASD is rather well-functioning.

The study population of those of at least 18 years of age (n=1266) was categorized according to current daytime activity. About one-fifth of this study population was found to be without any regular daytime activity (n=269), and the remaining young adults were engaged in so-called normative education/occupation (n=567) or customized education/occupation (n=430). The individuals without regular daytime activity differed from the individuals in the other groups of daytime activity by experiencing more maladaptive behavior, anxiety, and depression, and lower levels of self- and proxy-reported QoL. The group in normative education/occupation differed from the individuals in the other groups of daytime activity by having the highest level of adaptive functioning, as well as self- and proxy-reported QoL; the lowest level of autism symptoms; and the lowest proportions of ID, maladaptive behavior, and psychiatric comorbidity. Furthermore, it was found that ID, part-time job, history of schooling in primary and lower secondary school, and availability of support were associated with groups of daytime activity, yet highest parental education was not.

QoL was investigated using the INICO-FEAPS Scale, which is customized for individuals with intellectual and/or developmental disabilities but has not previously been administered in an ASD study population. Therefore, the psychometric properties of the INICO-FEAPS Scale was investigated with analyses of internal consistency (average item total correlation, ordinal alpha, ordinal theta, McDonald's omega, and average variance extracted), internal structure using confirmatory factor analysis investigating a predefined model of eight correlated first-order factors, and convergent validity comparing results of the INICO-FEAPS with results from other QoL scales applying correlational analyses. Overall, acceptable psychometric properties of INICO-FEAPS were found by these analyses. QoL was explored for the entire study population. On a mean level, the lowest QoL domain scores were found for emotional well-being and interpersonal relationships. Scores varied for self-reports matched with proxy-reports, supporting earlier findings that these two types of reporting constitute different sources of information of QoL. Thus, it is important to gain insight into the subjective evaluation of QoL. Further, valid for both self- and proxy-reports, factors such as psychiatric comorbidity, ID, maladaptive behavior, sleeping difficulty, adaptive functioning, autism symptomatology, residence, and main daytime activity were found to be associated with QoL. However, the importance of each factor in QoL varied across individuals with ASD.

Overall, the results of this PhD project illustrate the heterogeneity of outcomes of adolescents and adults diagnosed with ASD in childhood, including both very well-functioning individuals and individuals more severely affected by behavioral problems, comorbidities, and low levels of adaptive functioning and QoL, in addition to apparent difficulties finding an appropriate daytime activity. Different factors were found to be associated with outcome – operationalized as QoL and groups of daytime activity – applicable for preparing the ground for future services and, in general, improving the lives of individuals with ASD.

DANSK RESUME

Det er gennem flere årtier blevet undersøgt, hvordan børn diagnosticeret med en autisme spektrum forstyrrelse (ASF) klarer sig senere i livet. Der er dog i tidligere undersøgelser ofte anvendt relativt små og selekterede studiepopulationer, ligesom et normativt perspektiv er blevet anlagt i vurderingen af, hvordan personerne klarer sig. Dertil er der kommet et øget fokus på livskvalitet hos unge og voksne med ASF. Tidligere undersøgelser har gentagne gange peget på, at hovedparten af unge og voksne med ASF klarer sig dårligt, uanset om der vurderes ud fra et normativt perspektiv, såsom at klare sig selvstændigt i hverdagen, eller om der vurderes ud fra et mere subjektivt perspektiv som livskvalitet. Da de diagnostiske kriterier for ASF er ændret og udbygget gennem tiden, er det ikke problemfrit at generalisere resultater fra studier med studiepopulationer diagnosticeret ud fra ældre diagnostiske systemer til ny-diagnosticerede børn med ASF. Med det formål at supplere og udvide den eksisterende forskning blev der i dette Ph.d. projekt udført en national spørgeskemaundersøgelse med inddragelse af forskellige parametre til vurdering af, hvordan personer diagnosticeret med ASF i barndommen klarer sig senere i livet.

Studiepopulationen i dette Ph.d. projekt blev identificeret i Danske Psykiatrisk Centralregister og blev, sammen med deres forældre, inviteret til at deltage i en spørgeskemaundersøgelse med fokus på generelt funktionsniveau, livskvalitet og nuværende dagsbeskæftigelse. Svarprocent for selvrapporteringer var 16,6% (n=933) og for forældrerapporteringer 30,8% (n=1734) resulterende i data fra 1881 unge og voksne med ASF med en gennemsnitsalder på 20,6 år, en gennemsnits-diagnosticeringsalder for ASF på 9,2 år og en kønsratio på 4.17:1. Data fra de danske nationale registre var tilgængelige for hele den inviterede kohorte, hvilket muliggjorde bortfaldsanalyser. I disse analyser blev den psykiatriske historik hos personer med ASF og sociodemografiske forhold for personer med ASF samt deres forældre sammenlignet. Der blev udelukkende fundet mindre forskelle mellem de personer, der besvarede undersøgelsen, og de personer, der ikke gjorde. Men der var en tendens til, at familier, hvori forældrene havde længere uddannelser og i højere grad var i beskæftigelse, mere hyppigt besvarede undersøgelsen. Studiepopulationen af unge og voksne med ASF blev dog i høj grad fundet repræsentative for personer diagnosticeret i barndommen med en autismediagnose ud fra ICD-10.

Studiepopulationen er blevet beskrevet i forhold til hyppighed af mental retardering (MR), psykiatrisk komorbiditet og problemadfærd, samt niveau af generelt funktionsniveau og omfang af symptomer på autisme, og der blev fundet stor variation indenfor studiepopulationen. Sammenlignet med tidligere studier var der dog en tendens til lavere hyppighed af problemadfærd og komorbiditet, samt et højere niveau af generelt funktionsniveau. Det indikerer, at en subgruppe af studiepopulationens unge og voksne med ASF er velfungerende på en eller flere af de undersøgte parametre.

De personer med ASF i studiepopulationen, som var mindst 18 år gamle (n=1266), blev kategoriseret i forhold til nuværende dagsbeskæftigelse. Omkring en femtedel af gruppen havde ingen regulær dagsbeskæftigelse (n=269), og de resterende unge voksne i gruppen havde såkaldt normativ uddannelse/beskæftigelse (n=567) eller en form for tilpasset uddannelse/beskæftigelse (n=430). Personer uden regulær dagsbeskæftigelse adskilte sig fra de to øvrige dagsbeskæftigelsesgrupper ved at have en større hyppighed af problemadfærd, angst og depression samt lavere niveau af selv- og forældrerapporteret livskvalitet. Personer i normativ uddannelse/beskæftigelse adskilte sig fra de to øvrige dagsbeskæftigelsesgrupper ved at have det højeste niveau af generelt funktionsniveau samt selv- og forældrerapporteret livskvalitet, og den laveste hyppighed af MR, problemadfærd og psykiatrisk komorbiditet. Derudover viste analyser, at faktorerne MR, fritidsjob, skolehistorik gennem folkeskoleperioden samt tilgængelighed af støtte havde sammenhæng med dagsbeskæftigelsesgruppe. Forældres uddannelsesniveau havde ikke sammenhæng hermed.

Livskvalitet blev undersøgt med skalaen INICO-FEAPS, som er en skala tilpasset personer med intellektuelle og/eller udviklingsmæssige vanskeligheder. Denne skala har dog ikke tidligere været anvendt til personer med ASF. Derfor blev de psykometriske egenskaber af INICO-FEAPS undersøgt via analyser af intern konsistens, intern struktur ved brug af faktoranalyse med undersøgelse af en prædefineret model med otte korrelerede førsterangsfaktorer, samt konvergent validitet, hvor resultater fra INICO-FEAPS blev sammenlignet med resultater fra andre livskvalitetsskalaer med korrelationsanalyse. Samlet set blev der fundet acceptable psykometriske egenskaber for INICO-FEAPS i analyserne. Livskvalitet blev undersøgt for hele studiepopulationen. De laveste niveauer af livskvalitet blev fundet for domænerne emotionelt velbefindende og interpersonelle relationer. Derudover blev der fundet variation i selvrapporterede livskvalitetsscorer sammenlignet med matchede forældrerapporterede livskvalitetsscorer, hvilket er samstemmende med tidligere undersøgelser, som konkluderer, at de to typer af informanter udgør to forskellige kilder til information om livskvalitet. Derfor er den subjektive evaluering af egen livskvalitet væsentlig at få indsigt i. Gældende for både selv- og forældrerapporteringer blev der fundet sammenhæng mellem livskvalitet og faktorerne psykiatrisk komorbiditet, MR, problemadfærd, søvnvanskeligheder, generelt funktionsniveau, ASF-symptomer, bopæl og dagsbeskæftigelse. Men der var individuel variation ift., hvor stor betydning hver faktor havde for livskvaliteten.

Samlet set illustrerer de fundne resultater i Ph.d. projektet heterogeniteten i forhold til, hvordan unge og voksne diagnosticeret med ASF i barndommen har klaret sig. Der ses således meget velfungerende personer med ASF men også personer, som er præget af problemadfærd, komorbiditet og et lavt generelt funktionsniveau samt lav livskvalitet udover angiveligt at have vanskeligheder med at finde en passende dagsbeskæftigelse. Der blev fundet sammenhæng mellem en række forskellige faktorer og hhv. livskvalitet og dagsbeskæftigelse, hvilket er anvendelig viden til kommende indsatser og generelt forbedringer af livet for personer med ASF.

FUNDING

Several sources have supported this project financially. First, I would like to thank Aalborg University Hospital and the Psychiatry Department, Aalborg University Hospital for providing financial support for planning the PhD project and for continuous support throughout the period of the PhD:

- Region Nordjyllands Sundhedsvidenskabelige Forskningsfond;
- Region Nordjyllands Pulje for Klinisk Psykiatrisk Forskning.

Additionally, several foundations have supported the project; I would like to thank:

- Helsefonden;
- Brødr. Hartmanns Fond;
- Aase og Ejnar Danielsens Fond;
- Sofiefonden;
- Fru C Hermansens Mindelegat;
- Oticon Fonden.

Overall, I would like to express my appreciation for every contribution received that helped me to conduct this research project.

ACKNOWLEDGEMENTS

During this project I have been supported in very different ways by a lot of people, and I would like to say thank you to you all.

Thank you to all the participating parents and adolescents and adults with ASD, who were willing to share information about their lives and to put time and effort into completing the survey.

I would also like to thank my supervisors, Dr Med. Marlene Briciet Lauritsen and psychologist Gry Kjærsdam Telléus PhD for supporting me in this project from the very beginning, and for supervision when needed during the entire period of the PhD.

Several people offered different kinds of valuable practical assistance in execution of the project. I would like to thank my friend Lena Andersen for preparing the logo for the AutCome study, and psychologist Mark Self for back-translation of the scales used in the survey. I would also like to thank psychologist and friend Rikke Steensgaard for reviewing the survey material, and for valuable discussions about selection of material and interpretation of results. Further, I would like to thank Professor Lisa Ruble and PhD student Venus Wong, University of Kentucky, USA, for advice on the parent empowerment concept and for lending me their parent empowerment scale. Additionally, I would like to thank psychologist Lennart Pedersen, from *Center for Autisme*, Herlev, for support in conducting the survey, offering guidance and direction in construction of the questionnaires, and advertisement of the survey on the homepage of the *Center for Autisme* website. Similarly, I would like to thank President Heidi Thamestrup of *Landsforeningen Autisme* for support in conducting the survey and for advertising the survey in the journal. Special thanks go to Professor Sven Bölte and psychologist and PhD student Soheil Mahdi, Karolinska Institutet, Stockholm, for letting me having a stay abroad at KIND and for letting me into the ICF project. It has all been very exciting and instructive.

I would also like to thank all my colleagues at my place of work, the Research Unit for Child and Adolescent Psychiatry, Aalborg University Hospital. A special thank you goes to statistician Helle Jakobsen, who, with patiences, has answered all my statistical questions and has provided invaluable help in performing the statistical analyses.

Last, but not least, I would like to thank my family. I thank my parents and parents-in-law for all kinds of practical help during the period of the PhD. Further, a special thank goes to my husband and my children for letting me work whenever needed and for encouragements during the entire process of the PhD project.

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LIST OF SCIENTIFIC PAPERS

This thesis is based on the following four papers:

I. Knüppel, A., Kjærsdam Telléus, G., & Lauritsen, M.B. (submitted). Description of a Danish nationwide survey of adolescents and adults diagnosed with autism spectrum disorder in childhood: The AutCome study.

The paper is in review and has been made available to the assessment committee.

II. Knüppel, A., Jakobsen, H., Lauritsen, M.B. & Kjærsdam Telléus, G. (in press). Psychometric properties of the INICO-FEAPS Scale in a Danish sample with autism spectrum disorder. *Research in Developmental Disabilities*.

The paper is accepted for publication and has been made available to the assessment committee.

III. Knüppel, A., Kjærsdam Telléus, G., Jakobsen, H., & Lauritsen, M.B. (submitted). Quality of life in adolescents and adults with autism spectrum disorder: Results from a nationwide Danish survey using self-reports and parental proxy-reports.

The paper is in review and has been made available to the assessment committee.

IV. Knüppel, A., Kjærsdam Telléus, G., Jakobsen, H., & Lauritsen, M.B. (in preparation). Characteristics of young adults with autism spectrum disorder performing different daytime activities.

The paper is in preparation and has been made available to the assessment committee.

ABBREVIATIONS

ABAS-II	Adaptive Behavior Assessment System-II
ADHD	Attention-deficit–hyperactivity disorder
ADI(-R)	Autism Diagnostic Interview(-revised)
ADOS-2	Autism Diagnostic Observation Schedule – second edition
APA	American Psychiatric Association
ASD	Autism spectrum disorder
AVE	Average variance extracted
CD	Coefficient of determination
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CI	Confidence interval
DALY	Disability-adjusted life year
df	Degrees of freedom
DPCRR	Danish Psychiatric Central Research Registry
DSM	Diagnostic and Statistical Manual of Mental Health Disorders
GAC	General Adaptive Composite Score (from ABAS-II)
ICD	International Classification of Diseases – Classification of Mental and Behavioral Disorders.
ID	Intellectual disability
IQ	Intelligence quotient
OR	Odds ratio

Other PDD	Other pervasive developmental disorder
PDD-NOS	Pervasive developmental disorder, not otherwise specified
PWI	Personal Wellbeing Index
QoL	Quality of life
RMSEA	Root mean square error of approximation
RRR	Relative risk ratio
SCQ	Social Communication Questionnaire
SD	Standard deviation
SRS	Social Responsiveness Scale
VAS	Visual analog scale
WAIS-IV	Wechsler Adult Intelligence Scale – fourth edition
WHO	The World Health Organization
WHOQOL -BREF	The World Health Organization quality of life – BREF (abbreviated 26-item version of the original 100-item WHOQOL scale)

TABLES AND FIGURES

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CHAPTER 1. INTRODUCTION

This chapter will provide an introduction to the history of autism as a concept, followed by a presentation of the former and current diagnostic classification systems, and an outline of the epidemiology of autism spectrum disorder (ASD). Furthermore, the composite results of previously conducted outcome studies for adolescents and adults with ASD are presented with outcome defined according to normative standards, as well as quality of life (QoL).

1.1. FROM A CLINICAL DESCRIPTION TO A FORMAL DIAGNOSIS: A HISTORICAL PERSPECTIVE OF AUTISM

In 1908 the Swiss psychiatrist Eugen Bleuler introduced the term "autism" to describe the aloof and withdrawn behavior of some of his patients (van der Gaag, 2017). Years later, Leo Kanner (1943) published his now well-known paper with clinical descriptions of 11 children with what he called "autistic disturbances." The characteristics of these children were described by Kanner as, for example, an inability to relate themselves to people and situations, an odd language development, marked limitations of spontaneous activity, sensory hypersensitivity, insistence on sameness, restricted interests, and stereotyped movements. Despite the described autistic disturbances, which diverged from the development of same-age peers, Kanner also described an unusual memory for certain objects as a distinctive strength. In this way Kanner also described the uneven cognitive profiles of these children. Almost simultaneously, but independently, Hans Asperger (1944), published a paper based on descriptions of four children, and he described the children as "autistic" when social reciprocity was significantly reduced. Asperger further characterized these children as having high but disharmonic intelligence and good verbal skills but with pragmatic language difficulties. Additionally, Asperger mentioned that many of these children as adults were able to attain a career in the field of science (van der Gaag, 2017). The descriptions provided by Kanner and Asperger resemble very well descriptions of children with different kinds and degrees of autism today, and their contributions are seen as the first thorough case descriptions of children with autism.

Following the case descriptions by Kanner and Asperger, efforts were made to systematically classify these children. This includes, for example, the progress report of a working party (1961), with Mildred Creak as chairman, where nine criteria for identifying children with what they called "schizophrenic syndrome" in childhood were listed. Later, Lorna Wing and Judith Gould (1979) investigated a system of classification of "socially impaired" children based on the quality of social interaction by clustering the social, language, and behavioral abnormalities of these children.

They recognized, as also indicated by Kanner and Asperger, that the quality of social interaction could be significantly affected, as seen in Wing and Gould's sample, where some children had both intellectual disability (ID) and impairments in social interaction, but these two areas of impairments also could exist independently of each other. Of note, Wing and Gould suggested that the abnormalities observed constituted a continuum of severity across the subgroups of socially impaired children, contrary to clearly separated categories. However, when classified in diagnostic classification systems, autism was from the outset considered a categorical disorder and not a dimensional classification of the disorder.

In 1967 The World Health Organization (WHO) included infantile autism as a diagnosis in the International Classification of Diseases (ICD), in the eighth revision of the system (ICD-8). However, infantile autism was listed under the grouping of psychoses, and first recognized as a separate category in ICD-9 in 1977 (Ousley & Cermak, 2014). Similarly, in 1968 the American Psychiatric Association (APA) operated with a childhood type of schizophrenia in the Diagnostic and Statistical Manual of Mental Health Disorders, second edition (DSM-II) (Ousley & Cermak, 2014), and with recognition of infantile autism as a separate category in the third revision of the DSM (DSM-III) (Baker, 2013). In DSM-III-R, DSM-IV, and DSM-IV-TR autism as a disorder was further defined by first expanding the number of diagnostic criteria and later the number of disorders to be included, for example Asperger's syndrome and Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS) (Baker, 2013). PDD-NOS has less stringent criteria for diagnosis and no requirement with regard to age of onset (van der Gaag, 2017).

In ICD-10, the most recent version of the ICD manuals, autism is defined as a group of pervasive developmental disorders characterized by "qualitative abnormalities in reciprocal social interaction and in patterns of communication, and by a restricted, stereotyped, repetitive repertoire of interest and activities" (World Health Organization, 1992) (p. 252). ICD-10 includes the diagnoses infantile autism, atypical autism, Asperger's syndrome, and two further diagnoses with fewer defined diagnostic criteria: Other Pervasive Developmental Disorder (Other PDD) and other pervasive developmental disorder, not specified. In DSM-5, published in 2013 by the APA, autism is now defined by a dimensional approach (American Psychiatric Association, 2013). Contrary to earlier editions of the DSM and also ICD, autism is now considered as a spectrum of disorders including two domains with requirements to specify the severity of each domain: "Persistent deficits in social communication and social interaction, and restricted, repetitive patterns of behavior, interests, or activities, with symptoms present in the early developmental period" (American Psychiatric Association, 2013) (p. 50–51). Additionally, for example, accompanying intellectual impairments must be specified. In comparison with DSM-IV, a diagnosis of ASD in DSM-5 has become more rigorous as there is less flexibility in the diagnostic criteria. Most importantly, it is required that a child must meet diagnostic criteria within both domains (Baker, 2013; van der Gaag, 2017). It is expected that the

forthcoming ICD-11, which currently exists in a beta draft, will apply a dimensional classification of autism as well and also apply the term ASD (ICD-11 beta draft, 2018). Generally, the term ASD is now widely acknowledged and will be used throughout this thesis when referring to the overall group of individuals with different kinds of autism.

1.2. EPIDEMIOLOGY OF AUTISM SPECTRUM DISORDER

Victor Lotter was the first to investigate the population-based prevalence of ASD by conducting a study of autism prevalence in 1966, applying purely behavioral criteria to identify children with autism (Evans, 2013). In this study, a prevalence rate of autism of 4.5 per 10,000 was found (Lotter, 1966). Since then, several prevalence studies have been published, demonstrating an increasing prevalence of ASD. In a review by Fombonne (2009), an estimation of the global prevalence of pervasive developmental disorders in childhood and adolescence, on the basis of 19 studies, was found to be 60–70 per 10,000. In this estimate, covering studies published in the period 2000–2008, the entire spectrum of autism was included. Similar results were found in another review, which found a global prevalence of ASD in childhood and adolescence of 62 per 10,000, and a more recent European prevalence estimate of ASD gives a median of 61.9 per 10,000 (Elsabbagh et al., 2012). The latter estimate was based on papers published since 2000, with the majority published since 2006. However, prevalence rates as high as 116.1 per 10,000 were found in a UK study (Baird et al., 2006), 181.1 per 10,000 in a Japanese study (Kawamura, Takahashi, & Ishii, 2008), and 2.2% in a South Korean study (Kim et al., 2014), all covering prevalence of ASD in childhood. Further, concentrating on adults, a recent UK study of prevalence of ASD gave an estimated prevalence of 11 per 1000 (Brugha et al., 2016). Overall, an increase in prevalence of ASD has been found since the first study of prevalence was published, with recent estimations of around 1% to as high as 2.2%.

Reasons for the rise in prevalence have been discussed. The origin of ASD is found to be strongly genetic (Gaugler et al., 2014). Furthermore, exogenous factors, for example exposure to toxic chemicals (e.g., pesticides, phthalates, air pollutants, heavy metals) in the prenatal period, or hypoxia during birth, have been found to be associated with the emergence of ASD (Mandy & Lai, 2016). However, the definition of the diagnostic criteria of ASD will obviously affect the prevalence estimate, where broader definitions of ASD according to the diagnostic criteria will result in more individuals fulfilling the criteria: the option given in ICD-10, implemented in 1994, to use, for example, the diagnosis “Other PDD” may result in an increase in prevalence compared with the options given in ICD-9, where ASD primarily existed as infantile autism. This was demonstrated in a Danish study investigating incidence rates of ASD in the period 1995–2010 using data from the Danish Psychiatric Central Research Registry (DPCRR) (Jensen, Steinhausen, & Lauritsen, 2014). In this study, the

incidence rates of all ICD-10 autism diagnoses increased during the period but they were more pronounced for the diagnoses Asperger's syndrome and Other PDD. This result indicated that diagnostic criteria impact on the prevalence of ASD; however, it is important to note that rates of all ICD-10 autism diagnoses increased, implying that diagnostic criteria alone might not explain the rise in prevalence.

The rise in prevalence might further be explained by, for example, the increase in knowledge of ASD in clinical practice, that the diagnostic label of ASD is needed by the families and individuals with ASD to receive sufficient services and support, and that society, in general, has moved from having a higher degree of predictability to requiring flexibility and fast information processing, resulting in individuals with so-called milder forms of ASD having impairments that did not exist to the same extent earlier on (Fombonne, 2009; van der Gaag, 2017).

With regard to sex distribution, a male predominance is found among individuals with ASD, independent of age. For children and adolescents, male:female ratios in the range of 1.4–16:1 were found in European studies published in the period 1966–2011 (Elsabbagh et al., 2012), and generally in the range of 2.8–8.3:1 in worldwide studies published in the period 2000–2008 (with the exception of a single study with a male:female ratio of 15.7:1) (Fombonne, 2009). Within these quite broad ranges, a Danish study found a male:female ratio of 3.85:1 using data from children, adolescents, and adults diagnosed in the period 1995–2010 (Jensen et al., 2014).

A *Lancet* report from 2016 showed the global burden of disease for ASD in terms of disability-adjusted life years (DALYs) to be lower than with other mental disorders such as depression and anxiety but higher than with other disorders with childhood onset such as conduct disorder and attention-deficit-hyperactivity disorder (ADHD) (Abajobir et al., 2017); the latter finding might partly be due to limited clinical or epidemiological evidence of remission from ASD versus that of ADHD (Baxter et al., 2015). Furthermore, a positive percentage change was found for DALYs for ASD from 1990 to 2016, and also when calculated for the period 2006–2016, even though this change was smaller (Abajobir et al., 2017). This illustrates an increase in DALYs for ASD the last few decades. Thus, overall the global burden of ASD is substantial; as a result, a growing need for knowledge about lifetime outcome and the different trajectories resulting in different outcomes is of high importance. Such knowledge gives rise to the establishment of adequate service and support for individuals with ASD in all age groups, in addition to knowledge about what to expect when having ASD or having a child with ASD.

1.3. OUTCOME STUDIES IN AUTISM SPECTRUM DISORDER

Rutter, Greenfeld, and Lockyer were the first to provide knowledge about outcome for ASD via a follow-up study on individuals diagnosed with autism in childhood (Rutter, Greenfeld, & Lockyer, 1967). In their study, outcome categories, ranging from very poor to poor to fair to good to normal, were introduced and applied to their sample consisting of 63 adolescents and adults with what the authors called infantile psychosis. The outcome categories were primarily based on normative standards; for example, to obtain a rating of normal outcome the individual should be living a normal social life and function at a satisfactory level at school or at work. According to this measure, 48% of the individuals had a poor outcome, and 9% had a normal or good outcome (Rutter et al., 1967). Yet, owing to difficulties with the exact operationalization of these outcome categories, Howlin and colleagues introduced a composite outcome rating score based on ratings of functioning at work, in friendships, and with independence (in living). The composite rating ranged from very poor to poor to fair to good to very good outcome (Howlin, Goode, Hutton, & Rutter, 2004). In their study, evaluating the outcome of 68 adults diagnosed with autism in 1950–1979, 12% had a very poor outcome, 46% had a poor outcome, 19% had a fair outcome, 10% a good outcome, and 12% a very good outcome (Howlin et al., 2004). Applying similar outcome categories, a Swedish population-based study of adults with autism born in the period 1962–1984 found that around 78% had a poor or very poor outcome (Billstedt, Gillberg, & Gillberg, 2005).

Subsequently, several studies applying one of these outcome ratings have been conducted, and a meta-analysis – including 15 studies with sample sizes varying from 16 to 197 and reporting an overall outcome rating for ASD – found that the long-term outcome is poor for about half of individuals (Steinhausen, Mohr Jensen, & Lauritsen, 2016). However, the results from a study by Farley et al. (2009) differ from this general finding. In their study, applying the outcome rating score proposed by Howlin et al. (2004), 24% of individuals achieved a very good outcome and another 24% achieved a good outcome. Farley et al. (2009) explained their findings partly by use of a population-based sample, and partly by the fact that the majority of the sample (93%) were members of the Church of Jesus Christ of Latter Day Saints thereby not only securing social inclusion of the individual with ASD, but also securing the provision of informal support to the family as a whole. Also, a study of adolescents and adults with Asperger's syndrome, primarily with an average or above-average level of intelligence, found so-called good and fair outcomes for 27% and 47% of the study population, respectively, indicating an association between intelligence and outcome (Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008).

The reasons for achieving a good outcome have been investigated, and it has generally been established that early language abilities and childhood intelligence are important in achieving a more positive outcome (Kirby, Baranek, & Fox, 2016; Magiati, Tay, & Howlin, 2014). However, overall, as concluded by Howlin et al. (2015), "almost

nothing is known about the factors that determine outcome" (p. 389). Similarly, research into additional factors, such as sex, childhood severity of autism symptomatology, childhood social functioning, and childhood psychiatric comorbidity and epilepsy, have not consistently been found to have any impact on outcome in adolescence and adulthood (Magiati et al., 2014). Additionally, there is a scarcity of investigations of associations between family and environmental factors extrinsic to the individual with ASD and adult outcome (Howlin & Magiati, 2017; Kirby et al., 2016). However, studies involving such contextual factors have been conducted, for example by Woodman, Smith, Greenberg and Mailick (2016) and Bal, Kim, Cheong and Lord (2015), indicating that factors related to the educational and family context, as well as early intervention, have a positive impact on adult outcome operationalized as daily living skills and/or proportions of maladaptive behavior and autism symptoms.

Several researchers have argued for estimating the outcome of individuals with ASD in broader terms as solely reaching the normative standards of society. For example, Ruble and Dalrymple (1996) argued that outcome in ASD should include an evaluation of how risk factors, as well as protective factors, lead to both competence (based on other's judgments) and QoL (a person's subjective perception). Likewise, Henninger and Taylor (2013) argued that both objective outcome criteria based on societal norms and more subjective perspectives of the individual with ASD should be taken into account, to produce a more multidimensional view on outcome for individuals diagnosed with ASD in childhood. Similarly, Burgess and Gutstein (2007) have argued for including a more subjective perspective such as QoL in the evaluation of adult outcome for individuals with ASD. Several samples of adults with ASD previously assessed applying the normative outcome rating (Billstedt et al., 2005; Howlin et al., 2004; Ruble & Dalrymple, 1996), reached a more positive outcome when QoL was assessed as outcome (Billstedt, Gillberg, & Gillberg, 2011; Moss, Mandy, & Howlin, 2017; Ruble & Dalrymple, 1996). As emphasized by Ruble and Dalrymple (1996), who found poor normative outcomes for adults with ASD: "despite their [adults with ASD] social and communication difficulties, however, many of the adults from the present study were working in valued jobs, participating in family and community activities, learning to make choices, and generally happy" (p. 8). Likewise, a poor outcome in terms of a lower functioning at work and a high degree of independence in living might not be equal to a poor life in general. However, reviews and a meta-analysis on studies of QoL in individuals with ASD provide less optimistic results, suggesting that individuals with ASD have a lower QoL than typically developing individuals (Ayres et al., 2017; Chiang & Wineman, 2014; Ikeda, Hinckson, & Krägeloh, 2014; Van Heijst & Geurts, 2015). Hence, generally, adult outcome of individuals diagnosed with ASD in childhood seem below typically developing individuals, regardless of the application of normative standards as outcome or a more subjective outcome rating as QoL.

In spite of the general findings, there are adolescents and adults with ASD who achieve more positive outcomes in terms of, for example, age appropriate adaptive functioning, or fulfilling mainstream educational goals (Kaboski, McDonnell, & Valentino, 2017; Rubin, 2005). This might be due to the enormous heterogeneity in cognitive, linguistic, social, and behavioral functioning found among individuals with ASD (Howlin & Magiati, 2017; Kaboski et al., 2017), apparently in addition to variability when it comes to contextual factors such as intervention received, services and support during childhood, and the quality of these initiatives. This heterogeneity is, however, a serious challenge in research, and, as emphasized by Howlin and Magiati (2017), much more systematic research is needed of lifetime outcome for individuals with ASD with the aim of finding and explaining trajectories of development. Conduction of systematic research includes the sampling of a relevant cohort of study participants. Owing to the heterogeneity of individuals with ASD the representativeness of a study sample is of high importance, in addition to the size of the sample. Further, there is a risk of inaccurate estimation of the outcome of newly diagnosed children if knowledge about outcome based on older individuals is applied (Kaboski et al., 2017). Hence, the characteristics of a certain ASD population will vary over time according not only to diagnostic criteria used, but also to the characteristics of the individuals referred to diagnostic evaluation (e.g., sex, age, level of functioning) in combination with societal characteristics (e.g., the need for a formal diagnosis to be appointed service). Thus, large-scale outcome studies are needed to enhance and update existing knowledge. Additionally, as stated by Kaboski et al. (2017), it is important to bear in mind that the first cohort of children diagnosed with ASD consistently and in a measureable manner according to diagnostic criteria and available assessment tools has only recently reached adulthood. Therefore, it is of relevance to conduct new studies following up adolescents and adults diagnosed with ASD in childhood.

CHAPTER 2. RATIONALE AND AIMS OF THE PHD PROJECT

2.1. OVERALL AIM OF THE PHD PROJECT

This PhD project was conducted with the aim of exploring outcomes on several parameters in a nationwide, population-based Danish sample of adolescents and adults diagnosed with ASD in childhood. The data used were derived from the autism outcome survey, AutCome, which studies I–IV are based on.

2.2. STUDY I

The purpose of Study I was to provide a methodological overview of the AutCome study, including a basic description of the study participants, and to give a thorough comparison of responders and non-responders of the survey with regard to sociodemographic factors, as well as factors related to the psychiatric history of the adolescents and adults with ASD. This work thus contributes with essential information on representativeness of the study sample, and thereby forms the basis for interpretation of subsequently conducted analyses focusing on specific outcomes for adolescents and adults with ASD.

2.3. STUDY II

One of the outcome measures studied in this PhD project is QoL, and several scales can be applied for the assessment of QoL. In the AutCome study, the INICO-FEAPS Scale was chosen owing to the customization of this scale to adolescents and adults with intellectual and/or developmental disabilities. However, the INICO-FEAPS Scale has not previously been administered in a sample of individuals with ASD. The aim of Study II was to investigate the psychometric properties of the INICO-FEAPS Scale when administered in a population of individuals with ASD, with regard to internal consistency, internal structure, and convergent validity.

2.4. STUDY III

The aim of Study III was to explore QoL in a population of adolescents and adults with ASD. First, levels of QoL in different QoL domains for both self-reports and parental proxy reports were examined, as well as the concordance between these two types of informant. Second, it was explored whether the level of QoL in this population was associated with different factors as follows: age at diagnosis, psychiatric comorbidity, sleeping difficulty, ID, maladaptive behavior, adaptive functioning, autism symptomatology, main daytime activity, and residence. These analyses were conducted with the overall intention of identifying possible areas of improvement in QoL for individuals with ASD.

2.5. STUDY IV

Study IV was performed with the aim of describing different types of current daytime activity of young adults with ASD, in addition to providing a comparison of the behavioral characteristics between groups of adults with ASD performing different types of current daytime activity. Furthermore, the aim of Study IV was to examine the association between contextual factors primarily related to schooling during primary and lower secondary school and type of current daytime activity. These analyses were performed to uncover and extend knowledge of conditions and experiences during life for young adults with ASD with different types of current daytime activity, including young adults without regular daytime activity.

CHAPTER 3. METHODS

The methods used in this thesis apply equally to studies I–IV and are, in part, described in each of these studies in accordance with the specific aim of each study. This chapter provides a thorough description of included participants and procedures followed. Further, it provides an overview of the scales and questions applied in the survey and the statistical analyses conducted.

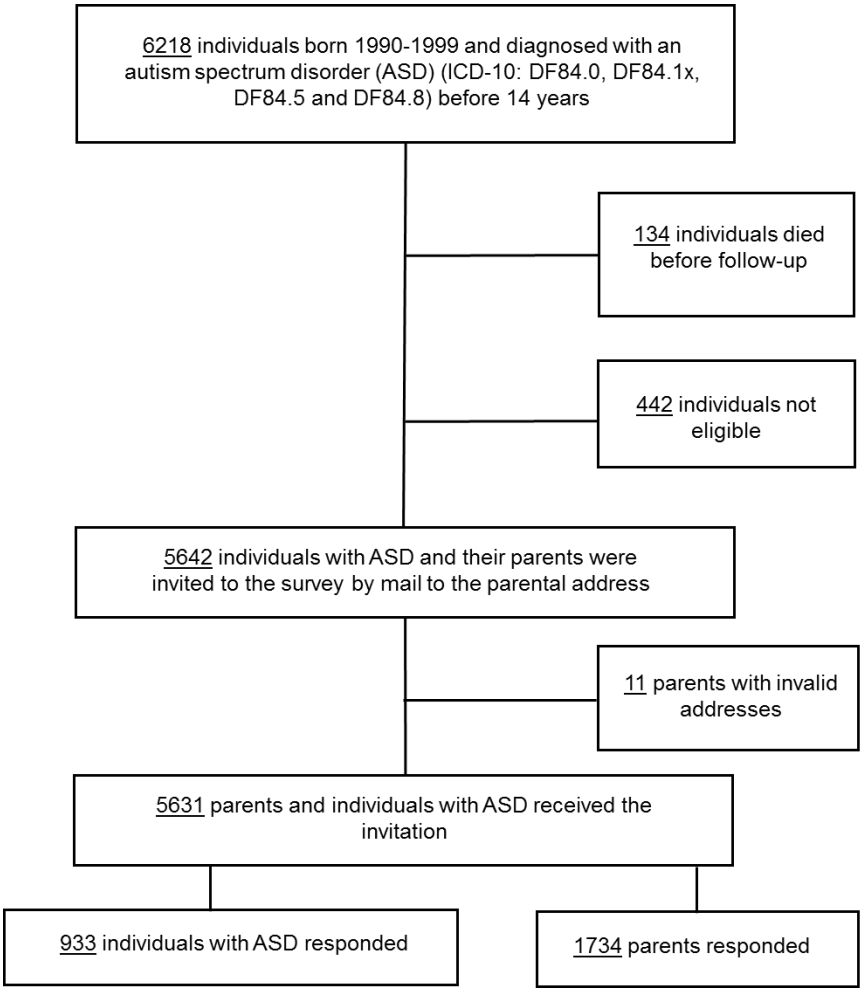
3.1. PARTICIPANTS

The participants included in this project were born in the period 1990–1999 and diagnosed with ASD at Danish psychiatric hospitals for children and adolescents before the age of 14 years. The DPCRR (Mors, Perto, & Mortensen, 2011) was used for identification of the participants assessed in outpatient or inpatient settings and diagnosed with one of the following diagnoses, according to ICD-10 (World Health Organization, 1992): F84.0 Infantile Autism, F84.1x Atypical Autism, F84.5 Asperger's Syndrome, and F84.8 Other PDD. In case an individual was registered in the DPCRR with more than one ASD diagnosis, the first diagnosis was selected. The ICD-10 diagnosis other pervasive developmental disorder, not specified (F84.9) was not included owing to the, at least in some psychiatric hospitals, temporary use of this diagnosis in connection with the psychiatric assessment. Hence, it would not have been possible to determine, for example, whether an individual had solely been assessed for an ASD diagnosis but did not fulfill the criteria for ASD after psychiatric assessment. Individuals who had received a register-based ICD-8 (World Health Organization, 1967) diagnosis of ASD (299.00, 299.01, and 299.02) were included, but the parents were only given the possibility to mark an ICD-10 diagnosis of ASD or to write the ICD-8 diagnosis themselves in the survey. ICD-10 was implemented as of 1994 (Mors et al., 2011), making it very likely that only a few individuals were diagnosed with an ICD-8 diagnosis. In addition, owing to the fact that outpatients were registered in the DPCRR from 1995 (Mors et al., 2011), there might be a small group of individuals born in the early 1990s and diagnosed with ASD in early infancy in outpatient settings who are not included.

Participants were invited to take part in the survey, together with their parents, via a mailing sent to the parent's addresses. The mailings included separate invitations and information sheets for the parents and the adolescent/adult with ASD. Therefore, only individuals with ASD whose parent(s) were alive and currently had a valid Danish postal address were invited. Moreover, owing to Danish privacy laws, only families where the parent(s) had custody of the child(ren) at the time of diagnosis of ASD were invited. Accordingly, a small group was not eligible and could not be invited for to the abovementioned reasons (i.e., parent(s) not alive, parent(s) had invalid postal

address, parent(s) did not have the custody of the child at the time of diagnosis of ASD). However, as illustrated in Figure 1, the majority of the cohort of Danish adolescents and adults registered with a diagnosis of ASD and their families were invited to participate in the survey.

Figure 1: Flowchart of participants in the AutCome study (Study I).



3.2. SURVEY PROCEDURE

As briefly described in Study I, families were invited by mail to participate in an online self-administered survey using the platform SurveyXact. Parents and adolescents/adults were each issued with unique logins. Completion of the questionnaire in one sitting was not required; responders could login to their partially completed, saved, questionnaires as many times as they required. If preferred, the parents and/or the individual with ASD could receive a paper edition of the questionnaire(s) and return it/them after completion. A single giveaway was provided in a lottery available to responders. Parents could choose to complete the questionnaire together or alone. Additionally, parents were allowed to assist their son/daughter in completing the survey, but it was emphasized that their son/daughter should decide how to answer the questions themselves. Support in completing the questionnaires was available by telephone and e-mail, and a reminder was sent out once by mail. The survey was open for 2 months, but a few families completed the survey shortly after the official deadline and these questionnaires were included in the final data set. It was not mandatory to complete every item in the questionnaire, but both respondent groups were encouraged not to skip any items. Prior to the launch of the survey, both questionnaires were piloted in a small sample of typically developing adults with expertise in the field of ASD or the Danish language. The questionnaires were revised according to comments received during this pilot study. Response rates were calculated for the parents and the individuals with ASD as the number of completed and partially completed questionnaires divided by the total number of potential participants, excluding the families for whom the letter was returned by the postal service owing to mismatch between name(s) and address (Figure 1; a total of 11 families).

3.3. DATA SOURCES

Data for the project were derived from two sources: survey data from the adolescents/adults with ASD and their parents, and register data from the Danish national registers.

3.3.1. SURVEY DATA

For each family two parallel surveys were available for completion: a self-report questionnaire and a questionnaire for the parent(s). With the purpose of reducing the workload of the individuals with ASD, the length of the questionnaire for self-report was considerably shorter than the parental questionnaire. For the self-report, all questions could be answered via check marks, which was also the case for the parental questionnaire, for the majority of the questions asked. However, in the parental version, text boxes were also inserted throughout the questionnaire to provide space

for parents to write comments or provide supplementary information concerning the topics addressed. Materials applied in the survey are listed and described in section 3.4.

3.3.2. REGISTER DATA

Data were gathered from the Danish national registers for the entire invited cohort. An overview of registers, register variables, and composite groups of register variables used in studies I–IV is provided in Table 1.

Register data covered, in particular, sociodemographic variables, in addition to date and year of diagnosis of ASD. If an individual was registered with more than one ASD diagnosis, data for the first registered diagnosis were extracted. To improve and expand the analysis of comparison of responders and non-responders of the survey, further register data from the DPCRR were used covering ASD diagnosis and the number of visits to psychiatric hospital departments, including both inpatient and outpatient care. A psychiatric hospital visit was defined as the period between date of admission and date of discharge at a psychiatric department. Register data from DPCRR concerning ASD diagnoses and psychiatric hospital visits on the individual level were not included in the dataset of the PhD project. Hence, Statistics Denmark performed analyses concerning these data and delivered the overall results.

Table 1 Overview of registers, register variables, and composite groups of register variables used in studies I–IV (Study I).

Description of register (Danish abbreviation of register name)	**Year**	**Population**	**Register variable(s) (variable description)**	**Definitions/eventual grouping of variable** (variable codes)
Psychiatric events from DPCRR (via LPR)	2014			
		ASD	c_diag* c_tildiag* c_adiag*	ICD-10 diagnostic code for (first) diagnosis of ASD (F84)**
		ASD	Date and year of (first) ASD diagnosis	
		ASD	d_inddto and d_uddto	Psychiatric visit/care: a period between date of admission and date of discharge at a psychiatric department (both inpatient and outpatient care)
Highest completed education (UDDF)	2014	Parents	HFAUDD converted to H1 codes (highest completed education)	1) No education (none of the codes listed below) 2) Primary and lower secondary education (10) 3) Upper secondary education (20, 25) 4) Post-secondary education and qualifying vocational education (35, 40, 50, 60, 65, 70)
Family income (FAIK)	2013	Parents	FAMSOCIOGRUP_13 (main occupation according to income, household)	1) At the labor market (110–114, 120, 131-135, 139) 2) Not at the labor market: unemployed, on sick pay, benefit from leave of absence (210, 220) 3) Not in the labor force I: disability pension, social security benefit (321, 330) 4) Not in the labor force II: retirement pension, early retirement, enrolled in education (310, 322, 323)
Relation to the labor market (AKM)	2013	Parents	SOCIO13 (main occupation according to income, individual)	1) At the labor market (110-114, 120, 131-135, 139) 2) Not at the labor market: unemployed, on sick pay, benefit from leave of absence (210, 220) 3) Not in the labor force I: disability pension, social security benefit (321, 330) 4) Not in the labor force II: retirement pension, early retirement, enrolled in education (310, 322, 323)

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Description of register (Danish abbreviation of register name)	**Year**	**Population**	**Register variable(s) (variable description)**	**Definitions/eventual grouping of variable** (variable codes)
Information on the population (BEF)	2014			
		Parents and ASD	KOM (municipalities)	I) Municipalities grouped into Danish regions *** 1) Capital 2) Central part of Jutland 3) Northern part of Jutland 4) Zealand 5) Southern part of Denmark II) Municipalities grouped into density of population **** 1) Densely populated 2) Intermediate populated, town with ≥40,000 inhabitants 3) Intermediate populated, town with <40,000 inhabitants 4) Intermediate populated, town with <15,000 inhabitants 5) Thinly populated, town with ≥15,000 inhabitants 6) Thinly populated, town with <15,000 inhabitants
		ASD	Sex	
		Parents and ASD	Date and year of birth	

DPCRR: Danish Psychiatric Central Research Registry; ASD: autism spectrum disorder.
*ASD diagnoses from assessments at the emergency ward were excluded. **F84.2-F84.4 and F84.9 were excluded. ***Grouped according to official Danish geographical regional boundaries. ****Grouped via DEGURBA: Degree of Urbanization (Statistics Denmark, n.d.).

3.4. MATERIALS

The following materials were applied in both versions of the questionnaire (i.e., self-report and parental report). The self-report questionnaire was compounded by existing scales only. For the parental version of the questionnaire existing scales were applied whenever possible but supplemented with questions formulated specifically for this project. All scales used in the survey are further described in section 3.4.1. to 3.4.6. (and marked with *). The outline of each of the questionnaires is presented below.

Self-report questionnaire:

- Single-item QoL visual analog scale (VAS)*
- Personal Wellbeing Index (PWI) – intellectual disability*
- The INICO-FEAPS Scale*
- A single question concerning assistance in completing the questionnaire.

Parental questionnaire:

- Responder of the questionnaire (i.e. mother, father, both parents etc.)
- Current residence of their son/daughter
- Single-item QoL VAS*
- The INICO-FEAPS Scale*
- Schooling and current daytime activity:
  - Type of schooling from zero to tenth grade of their son/daughter (with inspiration from White, Scahill, Klin, Koenig, & Volkmar, 2007)
  - Evaluation of adequacy of services received during schooling at three time points (pre-preparatory classes, intermediate classes, lower secondary education classes) (with inspiration from White et al., 2007)
  - Accomplished education of the individual with ASD
  - Part-time job (with inspiration from Carter, Austin, & Trainor, 2012; Chiang, Cheung, Hickson, Xiang, & Tsai, 2012)
- Current daytime activity (educational, occupational, or other) of their son/daughter (with inspiration from Eaves & Ho, 2008; Taylor & Seltzer, 2012)
  - If work: match on, for example, educational level and interests between the individual with ASD and his/her occupation, specifications of working hours a week (with inspiration from Baldwin, Costley, & Warren, 2014; Taylor & Seltzer, 2012)
- The Adaptive Behavior Assessment System-II (ABAS-II)*
- The Ritvo Autism and Asperger Diagnostic Scale-Revised – 14 Screen (RAADS-14 Screen)*
- Behavioral, psychiatric, and somatic conditions:
  - Behavioral problems and other difficulties (destructive including self-destructive, defiant, disrupting, anxiety, hurtful to others, socially offensive,

sadness, repetitive, sleeping and eating problems) (with inspiration from Ruble & Dalrymple, 1996)
    - ASD diagnosis of their son/daughter
    - Psychiatric comorbidity at three different time points (before the ASD diagnosis, contemporary with the ASD diagnosis and after the ASD diagnosis) (with inspiration from Eaves & Ho, 2008; Farley et al., 2009)
    - Other: presence of ID, epilepsy, vision impairments, hearing impairments, motor impairments, language impairments
- Support and services (with inspiration from Eaves & Ho, 2008):
    - Services and/or interventions received allotted to the individual with ASD and/or the family at 3–5 different time points, depending on the age of the individual with ASD (preschool age, age equaling pre-preparatory class, age equaling intermediate class, age equaling lower secondary education class, age equaling period between lower secondary education class and the age of 18 years, 18 years or older)
    - Evaluation of adequacy of services and/or intervention received directed at the individual with ASD and/or the family for each time point as listed above
- A subscale from The Parent Activation, Advocacy and Empowerment Scale.*

3.4.1. SINGLE-ITEM QOL VAS SCALE

A single-item QoL VAS covered "overall satisfaction with life." This item corresponds to the optional item described in the PWI (International Wellbeing Group, 2013), and similar items are frequently used in different research settings (de Boer et al., 2004; Tilford et al., 2015). The item is rated on a 0–10 scale, with a higher score indicating a higher QoL, and the rating was visually supported by smileys at each end of the scale.

3.4.2. PWI – INTELLECTUAL DISABILITY

PWI – intellectual disability (Cummins & Lau, 2005) is a QoL scale including seven items. The intellectual disability form of the PWI was used owing to the more concrete wording; however, the pre-testing protocol was not applied. The scale is designed as the first level of deconstruction of QoL as a whole with each item corresponding to a QoL domain. Each item is rated on a VAS ranging from 0 to 10, in this project visually supported by smileys at each end of the scale. A total score consists of the sum of the item scores (range 0–70), with a higher score indicating a higher QoL.

3.4.3. THE INICO-FEAPS SCALE

As stated in Study II, the INICO-FEAPS Scale (Gomez, Verdugo, & Arias, 2015) is used to assess QoL in individuals with intellectual and/or developmental disabilities. The scale features two different forms: a self-report form to be completed by the individual, and a report of others form to be completed by another person. Both forms

of the scale consist of 72 items divided into eight subdomains: self-determination, rights, emotional well-being, social inclusion, personal development, interpersonal relationships, material well-being, and physical well-being. The content of each item is the same across the two forms of the scale. Each item is measured on a Likert scale, with scores ranging from 1 to 4, and domain scores are calculated by summing the total scores of each of the nine items (range 9–36). The total score consists of the sum of each domain (range 72–288) with a higher score indicating higher QoL. In the self-report form there were both written and visual instructions for completing the scale; the report of others has written instructions only. As described for Study II a few modifications were made to the scale to ensure usability for the study population in this project, including individuals managing to live without support or with minor support only. However, these alterations were not considered to change the INICO-FEAPS Scale to an extent where the Danish version of the scale is not comparable with the original scale. Ordinal alpha was calculated for both versions of the instrument and found to be in the range 0.658–0.898 for the domains in self-report, and 0.733–0.896 for the domains in report of others, overall indicating an acceptable internal consistency (for details, see Study II).

3.4.4. ABAS-II

The ABAS-II was applied for a comprehensive assessment of adaptive behavior and skills (Harrison & Oakland, 2004). The adult form (aged 16–89 years) was used. The ABAS-II features nine domains (communication, community use, functional academics, home living, health and safety, leisure, self-care, self-direction, and social) and an additional optional domain (work), which was not applied in this project. The Danish version of the ABAS-II was translated by the *Center for Autisme*, which is a national center performing diagnostic assessments, consulting, and offering courses to people with autism and their families in addition to professionals. ABAS-II is widely used in Denmark when assessing adaptive behavior and skills in adolescents/adults with ASD. A total score can be calculated and summarized as the general adaptive composite (GAC) score, which has a mean of 100 (standard deviation (SD)=15). A higher score indicates better adaptive functioning. For each domain in ABAS-III, ordinal alpha was calculated and found in the range of 0.961– 0.986, indicating acceptable internal consistency within each domain.

3.4.5. RAADS-14 SCREEN

The RAADS-14 Screen is developed for assessment of autistic symptoms, and is based on the Ritvo Autism and Asperger Diagnostic Scale-Revised (Eriksson, Andersen, & Bejerot, 2013). It contains three domains: mentalizing deficits, social anxiety, and sensory reactivity. Originally, it was created and validated as a self-report instrument, but in this study it was used for parental report. Although the instrument has not been validated for parental reports, it has been piloted in a small sample of parents of adults with ASD with good results (J.M. Eriksson, personal

communication, May 16, 2015). In the RAADS-14 Screen the response alternatives to each of the 14 items illustrates the duration of each symptom, ranging from "never true" to "true only when he/she was younger than 16" to "true only now" to "true now and when he/she was young." Each item is scored on a Likert scale ranging from 0 to 3, and the sum of the item scores constitutes the total score with a higher score indicating more ASD symptoms (range 0–42). For screening purposes, a cut-off score of 14 is suggested (Eriksson et al., 2013). One of the response alternatives was slightly modified owing to the fact that a subgroup in this study population was 16 years old, making it difficult to use the alternative response "true only when he/she was younger than 16." For that reason, the age of 16 years was changed to 15 years. For each domain in RAADS-14 Screen ordinal alpha was calculated and found to be 0.674, 0.720, and 0.882, respectively, indicating an overall acceptable internal consistency.

3.4.6. THE PARENT ACTIVATION, ADVOCACY AND EMPOWERMENT SCALE

Parent empowerment was assessed with a 20-item subscale from the Parent Activation, Advocacy and Empowerment Scale. The scale is currently under development by a research group from University of Kentucky, USA, and, for that reason, the results from this scale are not utilized in studies I–IV. It is being developed for parents of adolescents/adults with various disabilities (L. Ruble, personal communication, April 13, 2015).

3.4.7. INSTRUCTION AND PROCEDURE IN QUALITY OF LIFE ASSESSMENT

In order to gather the most subjective data on QoL as possible for adolescents/adults not able or willing to provide self-reports, parents were instructed to rate their son's/daughter's QoL as they thought their son/daughter would rate it themselves (i.e., proxy-reporting). Compared with standard parent report, proxy-report of QoL is closer to the subjective rating of QoL done by self-report (Hong, Bishop-Fitzpatrick, Smith, Greenberg, & Mailick, 2016; Sheldrick, Neger, Shipman, & Perrin, 2012). Following the recommendation of the International Wellbeing Group (2013), the order of the QoL scales in the questionnaires was as follows: the single-item QoL VAS scale, PWI – intellectual disability (self-report only), and the INICO-FEAPS Scale.

3.4.8. TRANSLATION OF MATERIALS

Translation of the INICO-FEAPS Scale, RAADS-14 Screen, PWI, and the parent empowerment subscale into Danish was conducted according to the procedure mentioned in Study II. The procedure following forward- and back-translation was applied. The aim was to develop Danish versions of the scales using an easily

accessible Danish language and with a content conceptual equivalent to the original versions.

3.5. CODING OF SURVEY DATA

For some categorical variables originating in the survey, the answers provided were used in crude data analysis. This applied, for example, to yes/no answers (e.g. “did your child had a part-time job at any point?”). Yet, for some categorical variables, data were coded according to the aim of the specific data analysis (the coding procedure is described in studies I–IV). An overview of the categorical variables applied in and coded for use in studies I–IV is found in Table 2.

Table 2 Overview of studies with coding procedure described.

Variable(s)	Study in which coding is described			
	I	II	III	IV
Residence		X	X	
Psychiatric and/or somatic conditions	X		X	X
Maladaptive behavior			X	X
Schooling				X
Current daytime activity		X	X	X
Support and services				X

3.6. ETHICAL ASPECTS

Invitations for the parent(s), as well as for the adolescent/adult with ASD, were mailed to the parental postal address. The reason for inviting the individuals with ASD via their parents was that some adolescents/adults diagnosed with ASD in childhood might not be aware of their diagnosis. This issue was also recognized in a follow-up study by Cederlund et al. (2008), and it was considered to be unethical to reveal any unknown information contained in the invitation to the individual with ASD. Furthermore, parents had the option of rejecting the invitation on behalf of their child in case it would be too stressful for their child to complete the questionnaire. It was clearly described in the mailed information sheets that participation in the survey was voluntary, and that non-participation would not affect access to services and intervention henceforth. Furthermore, it was stressed that if the individual with ASD preferred their parents not to participate, it should be accepted by the parents. The families were informed why they were contacted, and from where their names and postal address were obtained.

The project was registered with the The Danish Data Protection Agency (record no. 2008-58-0028). Preceding an application and approval process, The Danish Health Data Authority provided the parental addresses used to invite the study population. Permission to use the instruments and scales was obtained prior to including the selected scales and instruments in the online survey, and data were anonymized prior to statistical analysis.

3.7. STATISTICAL ANALYSES

The statistical analyses performed are described in detail in studies I–IV. In general, missing values in INICO-FEAPS, ABAS-II, and RAADS-14 Screen were handled with multiple imputation, with five imputations for each missing value. However, in Study II other methods for handling missing data in INICO-FEAPS were applied in whatever method fitted the conducted analysis (for details, see Study II). A maximum was set for missing values for each scale: one missing value in each domain in INICO-FEAPS, two missing values in each domain in ABAS-II, and one missing value in RAADS-14 Screen. Overall, proportions of missing values according to total number of values was 0.20% for INICO-FEAPS self-reports, 0.35% for INICO-FEAPS report of others, 0.55% for ABAS-II, and 0.31% for RAADS-14 Screen. To some extent missing data for other variables exist in the survey, resulting in a variable number of observations in the analyses performed. For that reason, the total sample size (n) for each analysis is always specified.

For estimation of internal consistency of the applied scales, ordinal alpha was calculated (Gadermann, Guhn, & Zumbo, 2012). The statistical methods applied for evaluation of the psychometric properties of the INICO-FEAPS Scale when administered in a sample of individuals with ASD are described in Study II. Yet, for the majority of analyses conducted in Study II, the approach of the developer of the INICO-FEAPS Scale (Gomez et al., 2015) was replicated. For description of the study sample, descriptive analyses, including frequencies, means, and dispersions, were calculated. Comparisons between groups were undertaken using independent *t*-tests, χ^2, or Fischer's exact tests, the last two combined with Cramer's *V* for estimation of the magnitude of effect size. The thresholds for small-, medium-, and large-effect size according to Cohen (1988) were applied: for degrees of freedom (df) =1 (small=0.10; medium=0.30; large=0.50); for df=2 (0.071; 0.212; 0.354); for df=3 (0.058; 0.173; 0.289); for df=4 (0.050; 0.150; 0.250); and for df=5 (0.045; 0.134; 0.224). For associations between variables of interest, Pearson or Spearman correlation analyses were performed. For strength of correlation, the following thresholds were used: values from 0.30 to 0.50 indicate low correlation, from 0.50 to 0.70 moderate correlation, and from 0.70 to 0.90 high correlation (Mukaka, 2012).

Further, linear regressions and multinomial logistic regressions were performed. Independent variables in regression models were checked for multicollinearity, and

model fit was investigated through various fit indexes and inspection of residual plots. The result of the multinomial logistic regression analyses, a relative risk ratio (RRR), is commonly interpreted as an odds ratio (OR) (UCLA: Statistical Consulting Group, n.d.); hence, for a unit change in the predictor variable, the RRR of the outcome group relative to the base outcome group is expected to change by the estimated factor.

The significance level was set at $p<0.05$ for all analyses. Statistical analyses were carried out using IBM SPSS Statistics version 24 (IBM Corp., 2016), STATA version 14.2 (StataCorp., 2015a), and R version 3.2.5 (R Core Team, 2016), depending on the specific analysis and the performer of the analysis.

CHAPTER 4. RESULTS

In this chapter, the main results from studies I–IV are presented. The results are presented chronologically, starting with Study I and ending with Study IV, but divided into main themes. The study population can be considered as the total cohort invited to participate in the survey. Hence, in this thesis the term "study population" is used for the individuals with ASD for whom survey data are obtained.

4.1. SURVEY RESPONDENTS AND NON-RESPONDENTS

As presented in Study I, a total of 1734 parents and 933 individuals with ASD returned the questionnaire, corresponding to response rates of 30.79% (n=1734/5631) and 16.57% (n=933/5631), respectively (Figure 1). For 786 cases there were responses from both parents and the adolescent/adult with ASD. Both parents completed the questionnaire in 13.86% of cases (n=239/1724), the mother only in 77.26% of cases (n=1332/1724), the father only in 8.70% of cases (n=150/1724), and others (including other family members) in 0.17% of cases (n=3/1724). A total of 26.90% (n=230/855) of the adolescents/adults with ASD indicated that they had assistance in completing the survey.

Comparisons of responders and non-responders of the survey were conducted and described in Study I. These analyses were based on data concerning the individual with ASD and their parents. Responders were defined according to parental responder-status, that is, a parent-completed questionnaire with at least one usable answer. As described in Study I, there was no significant difference between responders and non-responders with regard to the sex of individuals with ASD ($\chi^2(1, n=5631)=0.02$, $p=0.902$), age of diagnosis of ASD ($t(5629)= –0.22$, $p=0.83$), number of psychiatric hospital visit(s) after the ASD diagnosis with maintenance of an ASD diagnosis in the record ($\chi^2(2, n=5631)=1.06$, $p=0.588$), and parental residence according to population density ($\chi^2(5, n=5631)=7.64$, $p=0.177$).

A significant difference combined with a below-small effect size was found for proportions of psychiatric hospital visit(s) before the ASD diagnosis ($\chi^2(1, n=5631)=5.00$, $p=0.025$, $V=0.0298$) with a higher proportion of responders with no visits (81.3% vs. 78.7%). For current mean age of individuals with ASD, a significant difference was found between responders (20.68 years, SD=2.74) and non-responders (20.31 years, SD=2.68) with a difference in mean of 4–5 months ($t(5629)= –4.70$, $p<0.001$). For current mean parental age, a significant difference was found between responders (51.09 years, SD=5.41) and non-responders (49.49 years, SD=5.41) with a difference in mean of about 1.5 years ($t(5629)= –10.27$, $p<0.001$).

Finally, a significant difference combined with an small effect size was found for the distribution of ICD-10 autism diagnoses (χ^2(4, n=5631)=15.01, p=0.005, V=0.0516), for parental residence according to the Danish geographic regions (χ^2(4, n=5631)=14.19, p=0.007, V=0.0502), for parental educational level (χ^2(3, n=5631)=109.20, p<0.001, V=0.1393), and parental main occupation according to income for the individual responder and household of the responder, respectively (individual: χ^2(4, n=5631)=67.64, p<0.001, V=0.1096; household: χ^2(4, n=5631)=77.22, p<0.001, V=0.1171). For responders, a larger number of individuals with ASD were diagnosed with Asperger's syndrome, and to a lesser degree diagnosed with, in particular, Other PDD than non-responders (Study I, Table 5). Furthermore, a smaller proportion of responding parents were from the capital region, in particular, and a larger number were from the central part of Jutland (Study I, Table 6). The largest effect sizes were found for comparisons between responders and non-responders with respect to the educational and occupational status of the parents. Thus, the parental responders tended to have achieved a higher educational level than non-responders and, to a higher extent, be in the labour market (Study I, Table 6).

In addition to the analyses performed for groups of responders and non-responders, additional information on the study population was obtained since a subgroup of invited individuals, primarily parents, via telephone or e-mail gave reasons for not completing the survey. Even though the number of inquiries was not formally counted, the majority was registered with the reason(s) for the inquiry. Based on these registrations (n≈100), the feedback was summarized into themes as follows:

- ASD diagnosis:
  - The ASD diagnosis was later re-evaluated and not confirmed.
  - The ASD diagnosis was not re-evaluated, but the parents felt confident that it was not valid.
  - The parents were not aware that their child were registered in DPCRR with an ASD diagnosis.
  - The parents and/or the adolescents/adults with ASD did not accept the diagnosis.
- The content and length of the questionnaire:
  - The parents found the questionnaire comprehensive or too difficult.
  - Parents of very low functioning or very high functioning grown-up children with ASD found the questions irrelevant to their situation.
- No exact up-to-date knowledge about the adolescent/adult with ASD:
  - The adolescent/adult with ASD was no longer living at home and had not done so for years. Additionally, in some cases the contact between the parents and the adolescent/adult with ASD was sparse.
- Refusals:
  - The adolescents/adults with ASD wanted no further confrontation with the ASD diagnosis.
  - The families felt unhappy about being invited.

- The parents did not have the energy/time to complete the survey at the appointed time for different reasons.

4.2. DESCRIPTION OF THE STUDY POPULATION

The study population consisted of a total of 1881 adolescents and adults with ASD with a mean age of 20.61 years at the time for the survey (range 16.50–26.48, SD=2.75). For 948 individuals parental reports only were available, for 147 individuals self-reports only were available, and for 786 individuals both parental and self-reports were available. Mean age of diagnosis of ASD was 9.22 years (range 1.05–14.00, SD=3.24), and male:female ratio was 4.17:1. The ABAS-II GAC score was found with a mean of 82.42 [SD=0.59; 95% confidence interval (CI): 81.27–83.57; range 40–120; n=1185]. For RAADS-14 Screen a mean score of 24.46 was found (SD=0.26; 95% CI: 23.95–24.97; range 0–42; n=1465). In Table 3, the frequencies of ICD-10 autism diagnoses, ID, and psychiatric comorbidity are presented for the total sample and for the sex-stratified sample. The most frequent ICD-10 autism diagnosis in the study population was Asperger's Syndrome (42.04%), followed by Infantile Autism (29.21%). A difference was seen across sex, where the proportions of Atypical Autism (14.59%) and Other PDD (15.30%) were higher among females than among males (Atypical Autism: 10.43%; Other PDD 11.01%), and the proportion of females diagnosed with Asperger's Syndrome was lower than for males (34.52% vs. 43.79%). ID was reported for 16.74% of the study participants (15.60% of males and 21.72% of females). Further, 43.65% of the study population was reported to have current comorbid psychiatric conditions, with a higher proportion of females (51.31%) than males (41.90%) having a comorbidity. Overall, the highest frequencies were found for ADHD/attention deficit disorder (19.18%), anxiety (9.69%), and depression (8.72%). As presented in Study I, the majority of the sample had a normal or near normal language function (92.38%, n=1369/1482), and a small proportion of individuals with current epilepsy (3.32%, n=49/1477). Maladaptive behavior, including behavior classified as self-destructive, hurtful to others, breaking belongings, defiant, disruptive, and/or socially offensive, was currently found for 29.17% (n=434/1488) of the study population and previously for 66.98% (n=990/1478) of the study population.

Table 3 ICD-10 autism diagnoses, intellectual disability, and psychiatric comorbidity in the study population (Study I).

	Total n (%)	Males n (%)	Females n (%)
ASD diagnosis			
Infantile autism	435 (29.21)	350 (28.97)	85 (30.25)
Atypical autism	167 (11.22)	126 (10.43)	41 (14.59)
Asperger's syndrome	626 (42.04)	529 (43.79)	97 (34.52)
Other PDD	176 (11.82)	133 (11.01)	43 (15.30)
ASD not classified according to ICD-10	85 (5.71)	70 (5.79)	15 (5.34)
Intellectual disability (ID)			
Minimal	58 (4.04)	43 (3.68)	15 (5.62)
Moderate	54 (3.77)	38 (3.26)	16 (5.99)
Severe	29 (2.02)	21 (1.80)	8 (3.00)
Unknown severity	99 (6.90)	80 (6.86)	19 (7.12)
Total ID	240 (16.74)	182 (15.60)	58 (21.72)
Psychiatric comorbidity			
ADHD/ADD	275 (19.18)	227 (19.45)	48 (17.98)
Tourette's syndrome	58 (4.04)	51 (4.38)	7 (2.62)
Learning disabilities	77 (5.37)	69 (5.91)	8 (3.00)
Anxiety	139 (9.69)	93 (7.97)	46 (17.23)
Depression	125 (8.72)	88 (7.54)	37 (13.86)
OCD	82 (5.72)	58 (4.97)	24 (8.99)
Eating disorder	27 (1.88)	17 (1.46)	10 (3.75)
Schizophrenia incl. other psychoses	27 (1.88)	24 (2.06)	3 (1.12)
Other disorder*	45 (3.14)	36 (3.08)	9 (3.37)
Unsure (parental reports)	53 (3.70)	45 (3.86)	8 (3.00)
No psychiatric comorbidity	808 (56.35)	678 (58.10)	130 (48.69)

Total sample size varies between 1434 and 1489.
ASD: autism spectrum disorder; Other PDD: other pervasive developmental disorder; AD(H)D: attention deficit (hyperactivity) disorder; OCD: obsessive compulsive disorder.
*This category contains other psychiatric disorders with a small number of participants each disorder.

4.3. PSYCHOMETRIC PROPERTIES OF THE INICO-FEAPS SCALE: QUALITY OF LIFE ASSESSMENT

In Study II, the psychometric properties of the INICO-FEAPS Scale were investigated according to internal consistency and internal structure, and further convergent validity was explored. A total of 875 individuals with ASD completed self-report forms, whereas 1573 report of other forms were completed. Internal consistency of

each domain of INICO-FEAPS was investigated using average item total correlation, ordinal alpha, and ordinal theta, and the internal consistency of each domain of the model – analyzed using confirmatory factor analysis (CFA) – was investigated using McDonald's omega and average variance extracted (AVE). Thresholds for values suggesting acceptable internal consistency were as follows: average item total correlation >0.3 (Nunnally & Bernstein, 1994); ordinal alpha, ordinal theta, and McDonald's omega >0.7 (Gadermann et al., 2012; Gomez et al., 2015); and AVE >0.5 (Hair, Ringle, & Sarstedt, 2011).

Overall, the domains of physical well-being and rights were found with the lowest internal consistency for both self-report and report of others. For self-report, values for physical well-being were found just below suggested thresholds for most indices applied (ordinal alpha=0.658; ordinal theta=0.671; McDonald's omega=0.625; AVE=0.358), whereas for report of others values for physical well-being were just below the suggested thresholds for indices calculated with CFA (McDonald's omega=0.656; AVE=0.403). The latter was the case for the domain rights for both self-report and report of others (self-report: McDonald's omega=0.654, AVE=0.389; report of others: McDonald's omega=0.592, AVE=0.353). Additionally, the value for AVE for the domain social determination in self-report was just below the suggested threshold (AVE=0.411). For the rest of the domains for both self-report and report of others, the values for the indices applied were either above the suggested thresholds (valid for average item total correlation, ordinal alpha, ordinal theta for both self-report and report of others, and in addition McDonald's omega for report of others), or very close to (self-report: McDonald's omega ≥0.670, AVE ≥0.443; report of others: AVE ≥0.482).

CFA was applied investigating a predefined model with eight correlated first-order factors (i.e., each domain of the scale corresponding to a factor). Summarized for self-report, the values of the goodness-of-fit indices were found as follows: χ^2=769.78 (p<0.001); root mean square error of approximation (RMSEA)=0.053; comparative fit index (CFI)=0.937; coefficient of determination (CD)=0.999. For report of others the following values of the goodness of fit indices were found: χ^2=1959.95 (p<0.001); RMSEA=0.070; CFI=0.914; CD=1.000. Overall, a slightly better fit of the model was found for self-report than for report of others when applying the often-used thresholds of RMSEA ≤0.06 (Hu & Bentler, 1999), CFI ≥0.95 (Hu & Bentler, 1999), and CD close to 1 (StataCorp., 2015b). For the χ^2 test, a non-significant result indicates a good fit, but the test is affected by a large sample size, and thus might be irrelevant to interpret for large study samples (Gomez et al., 2015; Russell, 2002). Lastly, convergent validity of the INICO-FEAPS Scale was explored with correlation analyses by comparing the total score of INICO-FEAPS with total scores of other QoL measurements administered in this project (PWI and the single-item QoL VAS). All possible correlations between the QoL measurements are given in Table 4.

Table 4 Correlations between different measures of quality of life (QoL; Study II).

Informant (QoL scale)		Correlation		n
Self-report (IF)	Report of others (IF)	0.64	*	710
Self-report (IF)	Self-report (VAS)	0.59	*	872
Self-report (IF)	Report of others (VAS)	0.47	*	739
Self-report (IF)	Self-report (PWI)	0.70	*	871
Report of others (IF)	Self-report (VAS)	0.31	*	740
Report of others (IF)	Report of others (VAS)	0.51	*	1567
Report of others (IF)	Self-report (PWI)	0.38	*	735
Self-report (VAS)	Report of others (VAS)	0.52	**	773
Self-report (PWI)	Self-report (VAS)	0.75	**	916
Self-report (PWI)	Report of others (VAS)	0.50	**	767

Proportion of imputed values in INICO-FEAPS: report of others: 0.26% to 0.34%; self-report: 0.19% to 0.26%.
IF: INICO-FEAPS Scale; PWI: Personal Wellbeing Index; VAS: single-item visual analog scale; n=sample size included in the analysis.
* Pearson correlation coefficient. ** Spearman correlation coefficient.

For investigation of convergent validity, the correlations between QoL estimates from the same informant group should be noted. Correlations between INICO-FEAPS self-report and other self-reported QoL estimates were positive and in the moderate range [single-item QoL VAS: $r(870)=0.59$; PWI: $r(869)=0.70$], and the correlation between INICO-FEAPS report of others and the single-item VAS was positive and also in the moderate range [$r(1565)=0.51$].

4.4. LEVELS OF QUALITY OF LIFE AND CONCORDANCE BETWEEN MATCHED RESPONDENTS

For all individuals completing the INICO-FEAPS Scale, four subgroups of informants were created in Study III: self-report with parental proxy report (n=710), self-report without parental proxy report (n=165), parental proxy report with self-report (n=710), and parental proxy report without self-report (n=863). Total and domain raw scores of the INICO-FEAPS Scale were linearly converted into a 0-100 point scale for easier interpretation (Cummins & Lau, 2005). As stated in Study III, the highest domain scores across respondent groups were found in the domains rights (range of means: 83.79–86.21), material well-being (range of means: 83.08–86.20), and for all subgroups of informants but one (proxy report without self-report) self-determination (range of means: 80.85–81.73) and personal development (range of means: 81.80–

82.24). The lowest domain scores across all respondent groups were found in the domains emotional well-being (range of means: 71.10–74.05) and interpersonal relationships (range of means: 65.07–71.88).

The concordance for matched respondents was investigated in Study III for INICO-FEAPS total score and domain scores. Matched respondents were defined as having both parental proxy reports and self-reports available for each individual with ASD (n=710). Correlation analyses showed positive correlations, overall in the moderate range [$r(708)=0.49$ to 0.61 between domains and $r(708)=0.64$ between total scores]. Furthermore, by applying regression analyses significant differences were found for matched respondents between INICO-FEAPS total score [$\beta=0.92$, $t(708)=1.99$, $p=0.047$] with a slightly higher score for self-reports than for parental proxy reports (79.40 vs. 78.48). Additionally, significant differences were found for matched respondents between domains scores for social inclusion [$\beta=3.38$, $t(708)=5.08$, $p<0.001$] and interpersonal relationships [$\beta= 5.85$, $t(708)=7.30$, $p<0.001$], with self-reports having higher scores than parental proxy reports (social inclusion: 79.00 vs. 75.62; interpersonal relationships: 71.88 vs. 66.02).

4.5. FACTORS ASSOCIATED WITH QUALITY OF LIFE

To examine whether a range of different factors were associated with QoL, linear regression analyses were performed for three respondent groups (self-report, and parental proxy report with and without matched self-report) with INICO-FEAPS total score as outcome, and the following independent variables: age of diagnosis of ASD, psychiatric comorbidity, residence, ID, main daytime activity, sleeping difficulty, maladaptive behavior, adaptive behavior, and autism symptomatology. The independent variables were inserted in the regression one at a time with adjustment for age and sex of the individual with ASD in each analysis (Study III). The results are presented in Table 5.

Table 5 Separate linear regression analyses with INICO-FEAPS total score as outcome for proxy reports subgroups and self-report (Study III).

	Self-report			Proxy report with self-report			Proxy report without self-report		
	Coef. (SE)	*p*	95% CI	Coef. (SE)	*p*	95% CI	Coef. (SE)	*p*	95% CI
Age of diagnosis of ASD (years)	–0.42 (0.09)	<0.001	[–0.59, –0.25]	–0.28 (0.11)	0.009	[–0.50, –0.07]	0.19 (0.11)	0.079	[–0.02, 0.40]
Psychiatric comorbidity	–3.07 (0.64)	<0.001	[–4.32, –1.82]	–5.09 (0.71)	<0.001	[–6.47, –3.70]	–4.49 (0.77)	<0.001	[–5.99, –2.98]
Residence									
Parents	–2.88 (0.99)	0.004	[–4.81, –0.94]	–4.91 (1.11)	<0.001	[–7.09, –2.72]	–6.14 (1.03)	<0.001	[–8.17, –4.11]
Outside family home with support	–3.95 (1.02)	<0.001	[–5.95, –1.96]	–6.83 (1.14)	<0.001	[–9.06, –4.60]	–11.39 (1.00)	<0.001	[–13.37,–9.42]
ID	–3.32 (1.00)	0.001	[–5.28, –1.35]	–6.65 (1.11)	<0.001	[–8.83, –4.46]	–9.10 (0.86)	<0.001	[–10.79,–7.41]
Main daytime activity									
Occupation	5.55 (1.13)	<0.001	[3.32, 7.77]	6.40 (1.26)	<0.001	[3.92, 8.88]	9.59 (1.08)	<0.001	[7.48, 11.70]
Education	4.41 (0.85)	<0.001	[2.75, 6.08]	6.89 (0.96)	<0.001	[5.02, 8.77]	11.06 (0.93)	<0.001	[9.24, 12.88]
Sleeping difficulty	–4.10 (0.63)	<0.001	[–5.33, –2.88]	–5.51 (0.70)	<0.001	[–6.88, –4.14]	–6.74 (0.73)	<0.001	[–8.17, –5.30]
Maladaptive behavior	–5.10 (0.70)	<0.001	[–6.47, –3.73]	–6.72 (0.77)	<0.001	[–8.24, –5.20]	–9.98 (0.72)	<0.001	[–11.41,–8.56]
Adaptive behavior	0.22 (0.02)	<0.001	[0.19, 0.25]	0.37 (0.01)	<0.001	[0.34, 0.40]	0.41 (0.01)	<0.001	[0.38, 0.43]
Autism symptomatology	–0.39 (0.03)	<0.001	[–0.45, –0.33]	–0.62 (0.03)	<0.001	[–0.68, –0.57]	–0.70 (0.03)	<0.001	[–0.76, –0.64]

Each analysis is adjusted for age and sex of the individual with ASD. Total raw scores of the INICO-FEAPS Scale were linearly converted into a 0-100 point scale.
A maximum of 0.52% of the total values in each analysis were imputed. Total sample size in each analysis varied from 546 to 875.
ASD: autism spectrum disorder; coef: unstandardized regression coefficient; SE: standard error; CI: confidence interval; ID: intellectual disability.
Definition of variables and Reference Group (RG): **Psychiatric comorbidity**=1 or more disorder(s), no disorders (RG); **residence**=living with parents, living outside family home with support, living independently without support (RG); **ID**=yes, no (RG); **main daytime activity**=involvement in any job-related occupation, enrolled in any education, no regular daytime activity (RG); **sleeping difficulty**=yes, no (RG); **maladaptive behavior**=yes, no (RG); **adaptive behavior**=composite score of ABAS-II (GAC); **autism symptomatology**=total score of RAADS-14 Screen.

As is evident from Table 5, the variable age of diagnosis of ASD did not have a significant association with QoL for the respondent subgroup parental proxy report without self-report, and in spite of significant associations for the other two subgroups of responders, the low regression coefficients should be noticed. For the remaining variables – psychiatric comorbidity, residence, ID, main daytime activity, sleeping difficulty, maladaptive behavior, adaptive behavior, and autism symptomatology – significant associations with QoL were found across respondent groups. As emphasized in Study III (illustrated in Figure 1 and Appendix 1a-c), variation in total INICO-FEAPS score was found within groups defined according to each categorical variable inserted in the regression analyses. Therefore, there seemed to be individual variation in how much a certain factor impacted on level of QoL for individuals with ASD.

4.6. CURRENT DAYTIME ACTIVITY OF YOUNG ADULTS

For individuals with ASD of at least 18 years of age (n=1266), categories of current daytime activity are presented in Study IV. Further, categories of current daytime activity were divided into three overall groups as presented below (adapted from Study IV).

- **Group 1: Individuals with a normative occupation or in education (n=567).**
  - Employment in community without support (n=111; 19.58%).
  - Post-secondary education (n=152; 26.81%).
  - Upper secondary or vocational education (n=304; 53.62%).

- **Group 2: Individuals with a customized occupation or in education (n=430).**
  - Employment in community with support (n=46; 10.70%).
  - Sheltered vocational setting (n=90; 20.93%).
  - Volunteering (n=4; 0.93%).
  - Primary and lower secondary school (degree-seeking) (n=53; 12.33%).
  - Customized educational program (degree-seeking) (n=193; 44.88%).
  - Other degree-seeking education (n=21; 4.88%).
  - Other non-degree-seeking education (n=17; 3.95%).
  - Folk high school (n=6; 1.40%).

- **Group 3: Individuals without any regular daytime activity (n=269).**

4.7. COMPARISONS OF DAYTIME ACTIVITY GROUPS

In Study IV, the young adults in the three overall groups of daytime activity were compared with regard to behavioral characteristics such as autism symptomatology, adaptive behavior, ID, maladaptive behavior, and psychiatric comorbidity. In addition to these variables, levels of QoL derived from the INICO-FEAPS Scale are compared herein. For continuous variables, linear regression analyses were performed (adaptive behavior, autism symptomatology, and QoL) with two regression analyses each variable with alternate reference groups. The results are presented in Table 6.

Table 6 Comparisons of daytime activity groups (Study IV, supplemented with total raw scores for INICO-FEAPS).

	Group 1 **Normative** mean [95% CI] (n)	**Group 2** **Customized** mean [95% CI] (n)	**Group 3** **None** mean [95% CI] (n)	**Regression 1*** **Group number; coefficient (*p*)**	**Regression 2*** **Group number; coefficient (*p*)**	**Group differences****
Autism symptomatology *(RAADS-14 Screen)*	19.82 [19.00, 20.65] (512)	27.87 [27.00, 28.73] (392)	27.88 [26.75, 29.01] (242)	1; –8.05 (<0.001) 2; –0.01 (0.987)	2; 8.04 (<0.001) 3; 8.05 (<0.001)	1 – (2;3)
Adaptive behavior *(ABAS-II, GAC)*	95.10 [93.53, 96.67] (425)	73.51 [71.44, 75.58] (318)	72.80 [70.28, 75.32] (192)	1; 22.30 (<0.001) 2; 0.71 (0.659)	2; –21.59 (<0.001) 3; –22.30 (<0.001)	1 – (2;3)
INICO-FEAPS *Self-report*	236.06 [233.24, 238.89] (262)	226.77 [223.56, 229.97] (179)	219.35 [214.94, 223.76] (114)	1; 16.71 (<0.001) 2; 7.42 (0.007)	2; –9.29 (<0.001) 3; –16.71 (<0.001)	1 – 2 – 3
INICO-FEAPS *Parental report*	237.98 [235.89, 240.06] (543)	215.11 [212.61, 217.60] (412)	203.38 [200.09, 206.67] (258)	1; 34.59 (<0.001) 2; 11.72 (<0.001)	2; –22.87 (<0.001) 3; –34.59 (<0.001)	1 – 2 – 3

ABAS-II GAC: adaptive behavior assessment scale II, general adaptive composite score; RAADS-14 Screen: The Ritvo Autism Asperger Diagnostic Scale-14 Screen; CI: confidence interval.

*Linear regression analyses with RAADS-14 Screen total score, ABAS-II GAC, or INICO-FEAPS total score as outcome. For regression 1, group 3 is the reference group. For regression 2, group 1 is the reference group. For RAADS-14 Screen 0.28% of the total values were imputed, for ABAS-II 0.56% of the total values were imputed, and for INICO-FEAPS 0.24% (self-report) and 0.36% (parental report) of the total values were imputed.

**Based on regression analyses with significant coefficient ($p<0.05$).

Group 1: in normative education/occupation; group 2: in customized education/occupation; group 3: no regular daytime activity.

As seen in Table 6, the individuals in the group in normative education/occupation differed significantly on level of autism symptomatology compared with individuals in the group in customized education/occupation and the individuals in the group without a regular daytime activity by having a lower mean score in RAADS-14 Screen (i.e., fewer autistic symptoms). For adaptive behavior the group in normative education/occupation also differed significantly from the group in customized education/occupation and the group without regular daytime activity by having a higher mean score on ABAS-II (i.e., better adaptive behavior). The group in customized education/occupation and the group without a regular daytime activity were not significantly different on levels of autism symptomatology and adaptive behavior. For QoL all groups differed significantly for both self-report and parental report with the highest level of QoL in the group in normative education/occupation and the lowest level in the group without a regular daytime activity.

Furthermore, whether differences existed between groups of daytime activity with regard to proportions of ID, maladaptive behavior, and psychiatric comorbidity was investigated. Fischer's exact tests were conducted combined with Cramer's *V* for estimation of effect size. A group difference was defined as a significant difference combined with a minimum small-effect size (Cramer's $V \geq 0.10$ or ≤ -0.10, df=1). These results are presented in Study IV (Table 4), with normative education/occupation as group 1, customized education/occupation as group 2, and no regular daytime activity as group 3. For ID, all groups of daytime activity differed [$p<0.001$, $V=0.42$ (group 1 vs. group 2); $V= -0.28$ (group 1 vs. group 3); $V=0.16$ (group 2 vs. group 3)], with the largest proportion of ID in the group in customized education/occupation (33.41%, n=138) and the lowest proportion in the group in normative education/occupation (2.60%, n=14). Similarly, all groups of daytime activity differed on proportion of current maladaptive behavior [$p\leq0.003$, $V=0.19$ (group 1 vs. group 2); $V= -0.30$ (group 1 vs. group 3); $V= -0.12$ (group 2 vs. group 3)] with the largest proportion in the group without daytime activity (44.31%, n=109), and the lowest proportion in the group in normative education/occupation (16.12%, n=84). For maladaptive behavior ever (i.e., lifetime), the group in normative education/occupation differed from the group without a regular daytime activity ($p=0.001$, $V= -0.12$) by having a smaller proportion of participants included [61.70% (n=319) vs. 74.29% (n=182)]. However, the group in customized education/occupation did not differ from the remaining groups with regard to lifetime maladaptive behavior [$p\geq0.017$, $V=0.08$ (group 1 vs. group 2); $V= -0.05$ (group 2 vs. group 3)]. For current psychiatric comorbidity, the group in normative education/occupation differed from the other groups [$p<0.001$, $V=0.14$ (group 1 vs. group 2); $V= -0.21$ (group 1 vs. group 3)] by having a larger proportion of individuals without psychiatric comorbidity (67.46%, n=342). Further, the group without a regular daytime activity had the largest proportions of anxiety (19.57%, n=46) and depression (17.87%, n=42), thereby differing from the proportions of these disorders in the other groups [anxiety: $p\leq0.003$, $V= -0.21$ (group 1 vs. group 3); $V= -0.12$ (group

2 vs. group 3); depression: $p \leq 0.001$, $V = -0.20$ (group 1 vs. group 3); $V = -0.14$ (group 2 vs. group 3)].

4.8. FACTORS ASSOCIATED WITH CURRENT DAYTIME ACTIVITY

Multinomial logistic regression analyses were performed in Study IV for investigations of factors associated with individuals in normative education/occupation or individuals in customized education/occupation relative to individuals with no regular daytime activity. Independent variables were inserted separately in the regression model with adjustment for age and sex of the individuals with ASD in each analysis. The following independent variables were investigated: parental highest education, ID, part-time job at any point, availability of current support, population density of the residence of the individual with ASD, and variables related to schooling during primary and lower secondary school (primary school type, schooling – hierarchical, school type of completion, number of school changes, and adequacy of support in school). Therefore, holding age and sex of the individuals with ASD constant, the risk ratio for being in the normative or customized group of daytime activity relative to the group without a regular daytime activity is estimated for each independent variable. RRRs for the variables investigated are found in Table 7, as well as results for Wald tests comparing RRR estimates for the group in normative education/occupation, and the group in customized education/occupation.

Table 7 Risk ratio for being in the normative or customized group of daytime activity relative to the group without a regular daytime activity (separate multinomial logistic regression models with the group with no regular daytime activity as base outcome; Study IV).

	Normative daytime activity				Customized daytime activity					Wald test on coefficients for normative vs. customized	
	RRR	SE	*p*	95% CI	RRR	SE	*p*	95% CI	n	$\chi^2(1)$	*p*
Parental highest education											
Primary and lower secondary school	0.52	0.18	0.064	[0.26, 1.04]	0.75	0.27	0.415	[0.37, 1.50]	1264	1.19	0.276
Upper secondary school	0.44	0.21	0.090	[0.17, 1.14]	0.61	0.30	0.310	[0.23, 1.59]		0.45	0.503
ID											
Present	0.12	0.04	<0.001	[0.06, 0.22]	2.22	0.43	<0.001	[1.52, 3.25]	1216	101.90	<0.001
Had a part-time job at any point											
Yes	3.67	0.61	<0.001	[2.64, 5.09]	0.89	0.17	0.536	[0.62, 1.29]	1255	95.73	<0.001
Availability of current support											
Yes	0.19	0.04	<0.001	[0.13, 0.29]	0.63	0.15	0.046	[0.40, 0.99]	1124	51.01	<0.001
No, but would like to	0.18	0.04	<0.001	[0.11, 0.28]	0.47	0.11	0.001	[0.29, 0.75]		28.55	<0.001
Population density											
Intermediate population density	0.70	0.13	0.052	[0.49, 1.00]	0.79	0.16	0.229	[0.53, 1.16]	1266	0.54	0.463
Thinly populated	0.58	0.11	0.005	[0.39, 0.85]	0.96	0.20	0.855	[0.64, 1.44]		9.60	0.002
Compulsory schooling											
Primarily in special education	0.38	0.06	<0.001	[0.28, 0.52]	1.89	0.34	<0.001	[1.33, 2.69]	1186	117.80	<0.001

Table continues on next page

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	Normative daytime activity				Customized daytime activity					Wald test on coefficients for normative vs. customized	
	RRR	SE	*p*	95% CI	RRR	SE	*p*	95% CI	n	$\chi^2(1)$	*p*
Schooling (hierarchical)											
Special, generic	0.26	0.07	<0.001	[0.15, 0.45]	2.27	0.78	0.018	[1.15, 4.47]	1151	59.75	<0.001
Special, autism	0.25	0.06	<0.001	[0.16, 0.39]	2.44	0.76	0.004	[1.33, 4.48]		85.41	<0.001
Completion of lower secondary school											
From special education, generic	0.27	0.08	<0.001	[0.16, 0.47]	3.84	1.29	<0.001	[1.99, 7.42]	937	93.20	<0.001
From special education, autism	0.17	0.04	<0.001	[0.11, 0.26]	2.92	0.85	<0.001	[1.65, 5.15]		137.99	<0.001
Number of changes of school											
1–2	1.00	0.21	0.996	[0.66, 1.51]	0.55	0.12	0.006	[0.36, 0.84]	1186	13.16	<0.001
≥3	0.56	0.13	0.015	[0.35, 0.89]	0.36	0.09	<0.001	[0.22, 0.58]		4.67	0.031
Adequacy of support in school											
Never or rarely adequate	0.65	0.10	0.004	[0.48, 0.87]	0.64	0.10	0.006	[0.47, 0.88]	1247	0.00	0.978

Each analysis is adjusted for age and sex of the individual with autism spectrum disorder.
RRR: relative risk ratio; SE: standard error; CI: confidence interval; n: sample size; ID: intellectual disability.
Definition of variables and Reference Group (RG): **parental highest education=** primary/lower secondary school, upper secondary school, post-secondary/vocational education (RG); **ID**=present, not present (RG); **part-time job**=yes, no (RG); **availability of current support**=available, no but would like to, unnecessary (RG); **population density=**intermediate population density, thinly populated, densely populated (RG); **compulsory schooling**=special education, mainstream education (RG); **schooling (hierarchical)**=special (generic), special (autism), mainstream (RG); **completion of lower secondary school**=special education (generic), special education (autism), mainstream education (RG); **number of changes of school**=1-2, 3-, 0 (RG); **adequacy of support in school during lower secondary school**=never/rarely adequate, adequate/not necessary (RG).

Regarding parental highest education no significant association(s) with group of daytime activity were found in any of the analyses conducted. Adults with ID were significantly less likely to be in the normative daytime activity group relative to the group without regular daytime activity (RRR=0.12), but significantly more likely to be in the group of adults with a customized daytime activity relative to the group without a regular daytime activity (RRR=2.22). Furthermore, the adults with ASD were significantly less likely to be in the normative or the customized groups of daytime activity, relative to the group without a daytime activity, if support for the individual with ASD and/or the family was needed (i.e., support evaluated as available or not available but needed). However, the upper bound of the 95% CI was very close to 1 for the customized group of daytime activity relative to the group without daytime activity for "support available" (0.99), indicating a possible small effect for this category.

Similar directed effects for variables related to type of schooling during primary and lower secondary school (compulsory schooling, schooling – hierarchical, school type of completion) were found for each group of daytime activity. Adults in normative education/occupation were significantly less likely to have attended special educational settings relative to adults without a regular daytime activity (i.e., RRRs <1), and adults in customized education/occupation were significantly more likely to have attended special educational settings relative to adults without regular daytime activity (i.e., RRRs >1). Additionally, the Wald tests conducted showed significant differences for RRRs for the variables of schooling for the group in normative education/occupation compared with the group in customized education/occupation. Comparing number of changes of school, adults in normative education/occupation (RRR=0.56), as well as customized education/occupation (RRR=0.36), were significantly less likely to have ≥3 changes of school compared with no changes relative to adults without a regular daytime activity. Furthermore, adults in normative education/occupation (RRR=0.65) and adults in customized education/occupation (RRR=0.64) were significantly less likely, relative to adults without a regular daytime activity to have evaluations of adequacy of support in school of "never or rarely adequate" compared with "adequate/not necessary".

CHAPTER 5. DISCUSSION

This chapter will summarize and discuss outcomes for adolescents and young adults diagnosed with ASD in childhood on the basis of results found in this PhD study. Further, considerations on assessment of QoL in populations of adolescents and adults with ASD will be discussed. Validity of the results is dependent on the validity of the ASD diagnoses of the individuals included in this study and the validity of the survey data; furthermore, the representativeness of the study population is important for generalization of the results. Reflections on these issues will be presented. A strengths and limitations section will end the chapter.

5.1. OUTCOMES FOR ADOLESCENTS AND YOUNG ADULTS WITH ASD

In studies I-IV, descriptive information to characterize the study sample was provided. Furthermore, supplements providing further descriptive information have been provided. Overall, this information included proportion of ID, language difficulties, psychiatric comorbidity, and maladaptive behavior, in addition to level of adaptive behavior.

5.1.1. OUTCOME RELATED TO BEHAVIORAL CHARACTERISTICS AND COMORBIDITY

For the study population the proportion with ID (independent of level of severity) was found to be around 17%. By comparison, it is often found that around half or more of study populations with ASD have ID (Ballaban-Gil, Rapin, Tuchman, & Shinnar, 1996; Billstedt et al., 2011; Eaves & Ho, 2008; Elsabbagh et al., 2012; Gray et al., 2014; Ruble & Dalrymple, 1996). However, several studies included populations of individuals with ASD without ID (Barneveld, Swaab, Fagel, Van Engeland, & De Sonneville, 2014; Farley et al., 2009; Renty & Roeyers, 2006), demonstrating that there is a group of individuals with ASD with intelligence within the average range. Yet, in these studies, individuals with ASD and ID are often excluded. The Autism and Developmental Disabilities Monitoring Network in the USA found that the percentage of 8-year-olds with ASD and with co-occurring ID varied widely from 20%-50% across nine states (Christensen et al., 2016). Furthermore, a Swedish epidemiological study of 0-17 year olds found that 23.6% of the study population with ASD also had ID (total n=10,025) (Xie et al., 2017), and a British epidemiological study of adults with ASD found an increase in prevalence rate from 1.0% to 1.1% when adults with ASD and ID were included (Brugha et al., 2016). These studies suggest that the proportion of individuals with ASD and ID might be smaller than

previously thought. However, the prevalence of ASD with and without co-occurring ID does not appear to have been thoroughly investigated.

The mean level of adaptive behavior (GAC score) for this study population was 82.42 (SD=0.59). The level of adaptive behavior may improve with age (Magiati et al., 2014), but compared with other studies applying scales of adaptive behavior in ASD study populations, the mean score of the study population in the present project generally seemed higher, with a total score around 1 SD below the mean versus around 2 SD below the mean in other studies (Hill, Gray, Kamps, & Enrique, 2015; Matthews et al., 2015; Wallace et al., 2016). However, large individual variability have been found for adaptive functioning (Magiati et al., 2014), and studies also exist that found mean scores of adaptive functioning comparable with the results in this PhD project (Kanne et al., 2011; McDonald et al., 2015). Study sample ascertainment will most likely impact on the level of adaptive functioning, as recently demonstrated for preschool children with ASD (Sacrey et al., 2017). In their study, children from a prospective cohort had higher adaptive functioning than a clinically referred cohort. Likewise, the level of adaptive functioning might be higher in a population-based sample than selected samples, for example clinically referred samples (e.g., Hill et al., 2015; Matthews et al., 2015).

For this study population, the proportion of individuals with language difficulties was around 8%, the proportion with current maladaptive behavior was around 29%, and the overall proportion of psychiatric comorbidity was around 44%. By comparison, the proportion of language difficulties is often found in the range of 20–30% (Levy & Perry, 2011), and the proportion of maladaptive behavior have been found to be around 40–50% or even higher in some studies (Ballaban-Gil et al., 1996; Billstedt et al., 2005; Farley et al., 2009). However, these estimates were based on different measures, making direct comparisons difficult. Further, the low proportion of ID, as well as language difficulties, in the study sample of this project might result in lower proportions of maladaptive behavior (Gray et al., 2012; Hill et al., 2014). Overall, psychiatric comorbidity has been found in a wide range, from 4% to 84% (Howlin & Moss, 2012; Levy & Perry, 2011); however, several studies have found psychiatric comorbidity to be in the range of around 50–80%, as discussed in Study I (Abdallah et al., 2011; Bishop-Fitzpatrick et al., 2016; Eaves & Ho, 2008; Farley et al., 2009; Gillberg, Helles, Billstedt, & Gillberg, 2016; Simonoff et al., 2008).

Overall, considering the results for the study population, it is suggested that the present sample included a larger subgroup of adolescents and adults with ASD, with a relatively high level of adaptive functioning and low proportions of behavioral difficulties and comorbid disorders than what previous studies have found. This might be a result of sampling a population-based study cohort, as well as inclusion of the broad range of autism diagnoses diagnosed via ICD-10 versus diagnostic systems used previously (Baker, 2013; Kaboski et al., 2017). Thus, the most well-functioning adolescents and adults diagnosed with ASD in childhood, who had evolved positively,

might be more difficult to find in clinically referred samples. However, it is evident that more severely affected individuals with ASD were included in the study population as well. Heterogeneity is often reported for individuals with ASD when it comes to, for example, functional abilities such as language and intelligence, and also the presence of symptoms compatible with comorbid psychiatric disorders (Georgiades, Szatmari, & Boyle, 2013). The large population-based sample recruited for this study may allow heterogeneity across individuals with ASD to be revealed, and the heterogeneity can be considered as an important aspect of understanding outcomes for adolescents and adults with ASD.

5.1.2. OUTCOME RELATED TO CURRENT DAYTIME ACTIVITY

Current daytime activities of individuals with ASD of at least 18 years of age were analyzed in Study IV. In this study, the proportion of individuals employed in the community without support was low [about 9% (n=111/1266; section 4.6.) for 18–26 year olds vs. 18–49% found in other studies (Barneveld et al., 2014; Gray et al., 2014; Howlin et al., 2004)]. However, the low employment rate found in the present sample might be a result of the large number of individuals attending normative education (36%, n=456/1266; section 4.6.), as well as customized degree-seeking education (21%, n=267/1266; section 4.6.). As level of education might increase the possibility of finding appropriate employment (Chen, Leader, Sung, & Leahy, 2015), the adults in the study cohort receiving an education might be employed at a later age, thereby increasing the low employment rate found at the time the study was conducted. Furthermore, the large number of adults with ASD receiving an education might improve the rates of individuals with ASD who complete education. As summarized by Levy and Perry (2011) previous studies have found that approximately 50–60% of adolescents and adults with ASD leave school without any formal qualifications. However, it is not yet possible to estimate the education completion rate in the project cohort.

As stated in study IV, it seems more relevant to compare the present results with other studies of individuals not participating in any regular daytime activity (i.e., no educational or occupational activities). The present sample included around 20% of 18–26 year olds (n=269/1266; section 4.6.) who were not currently enrolled in any education or engaged in any job. This proportion is relatively high compared with previous studies but is within the expected range, which is often reported from as low as <10% up to 20–40% (Barneveld et al., 2014; Cederlund et al., 2008; Farley et al., 2009; Gillespie-Lynch et al., 2012; Gray et al., 2014; Osada, Tachimori, Koyama, & Kurita, 2012; Taylor & Seltzer, 2012; Venter, Lord, & Schopler, 1992). However, a lower proportion of these individuals could have been expected owing to the overall smaller proportions of behavioral and comorbid difficulties and the relatively high level of adaptive functioning seen in the study population. Hence, it might be easier for individuals with ASD to access an appropriate daytime activity when the number of other difficulties is low.

Gray et al. (2014) reported on daytime activity for 89 adults with ASD (mean age 24.8 years; range 17.1–35.2) followed since childhood/adolescence. In their sample only 1% were without an organized daytime activity, yet around 75% had ID. In Taylor and Seltzer (2012), information on daytime activity for adolescents and adults with ASD was reported six times during a period of 12 years. At time 1, the individuals were a mean age of 22.84 years (range 10–52) and approximately 71% had ID. In their study, rates of no educational or occupational activities were low and relatively stable (range of 8.6–13.5%). These results suggest that having any daytime activity is not necessarily associated with presence of ID, hence frequencies for ID were high but the number of individuals without daytime activity was low. However, it can be assumed that having a daytime activity in terms of a job might be easier when intelligence is above the cut-off for ID (i.e., intelligence quotient (IQ) >70). As found by Howlin et al. (2004), adults with a childhood assessment of performance intelligence >70 had a better outcome operationalized as the overall outcome measure presented in the introduction, which, among others, takes into account daytime activity. However, as emphasized by Howlin et al. (2004), outcomes are variable among individuals with an IQ within the normal range, and, as demonstrated by Taylor and Seltzer (2011), individuals with ASD but without ID might even be at risk for being without a regular daytime activity. In their study, young adults with ASD but without ID were about three times more likely to have no regular daytime activity than young adults with both ASD and ID. The overall relatively low proportion of ID together with the relatively high proportion of no regular daytime activity found for the current study population may indicate similar findings. Hence, there might be a lack of variation in types of daytime activities for individuals with ASD but without co-occurring ID. Some of these individuals might be too well functioning for different types of existing customized daytime activities but still having too severe disability owing to their ASD and eventual psychiatric comorbidity to engage in daytime activity on ordinary conditions.

Further, it is important to bear in mind that the number of individuals with no regular daytime activity is most likely dynamic, varying with the state of the markets, access to appropriate education and jobs, and with available support for both education and occupation facilitating the path to a daytime activity. Additionally, there is no evidence that access to daytime activity improves with age. In a long-term follow-up study by Howlin, Moss, Savage and Rutter (2013), including 60 adults (mean age 44 years), the rate of no regular daytime activity was reported to be 55%. Follow-up of the present study sample will reveal any change in the proportion of individuals with ASD without regular daytime activity, including whether the individuals are only temporarily without a regular daytime activity or whether they tend to retain this status. However, it should also be taken into account that some individuals with ASD may need more time in education, and this might also include periods of no daytime activity. As stated by Marriage, Wolverton, and Marriage (2009), some individuals with ASD are reaching educational goals about a decade or more later than typically seen in the general population owing to their developmental delay.

As discussed in Study IV, the association between type of schooling during primary and lower secondary school and future daytime activity is, to date, not well explored and divergent results have been obtained (Chan et al., 2017; Chiang et al., 2012; Foster & Pearson, 2012; Venter et al., 1992; Woodman et al., 2016). Based on this PhD project, it is not possible to conclude that enrollment in a special type of schooling during primary and lower secondary school promotes any kind of future educational or occupational engagement. Hence, differences between groups of daytime activity were found, and the analyses are based on associations and are solely descriptive. However, tendencies in data emerged. Adults with ASD in normative education/occupation were more likely to have attended mainstream education than adults with ASD without a regular daytime activity. Furthermore, the adults with ASD in customized education/occupation were more likely to have attended a special educational setting than adults with ASD without a regular daytime activity. Additionally, RRRs found for variables of schooling were found to differ for the group in normative daytime activity and the group with a customized daytime activity. Hence, overall, adults with ASD taking part in a normative daytime activity seemed more likely to have attended mainstream school, and adults with ASD taking part in a customized daytime activity seemed more likely to have attended special educational settings. The adults without a regular daytime activity might have a position in between. However, as shown in Study IV (Table 5), almost 40% of the adults with ASD with a normative daytime activity had primarily been educated in special educational settings, and around 25% of the adults with ASD with a customized daytime activity (Study IV, Table 5) had primarily been in mainstream educational settings suggesting that the association between type of school and future daytime activity for adults with ASD is not a simple matter and should be explored further, as suggested in Study IV.

The young adults with ASD in the group without a regular daytime activity were more likely than those in the remaining groups with daytime activities to have experienced three or more changes of school during primary and lower secondary school, and, in addition, more likely to have experienced support in school, which was evaluated by their parents as never or rarely adequate. The adults without regular daytime activity might have been challenging to support sufficiently in the first choice(s) of educational settings, resulting in more changes in school. Importantly, highest parental education was not associated with the three groups of daytime activity. This result may, however, be distorted by the finding that the responders of the survey generally were from more socioeconomically advantaged families.

The very low proportion of ID (2.60%) in the group with a normative daytime activity versus the other groups of daytime activity should be noted (Study IV, Table 4). It is possible that less severe disability, in general, might have enabled a group of children to participate in mainstream education, but, unfortunately, childhood baseline information is not available in this project. However, parents were asked to rate whether their child had ever had maladaptive behavior, and, as presented in Study IV

(Table 4), high frequencies (around 62–74%) for lifetime maladaptive behavior were found for all individuals with ASD, independent of daytime activity, with lower frequencies for current maladaptive behavior (16–44% across daytime activity groups; Study IV, Table 4), indicating that the majority of individuals with ASD in this study population suffered from behavioral problems in childhood. This may also suggest different developmental pathways for individuals with ASD, even though the original starting point for some of them might have been identical (Kaboski et al., 2017). However, whether differences in baseline difficulties, as well as resources, were present in childhood and influenced the choice of type of school cannot be adequately investigated using the data in this survey.

5.1.3. OUTCOME RELATED TO QUALITY OF LIFE

Outcome for adolescents and young adults with ASD was also evaluated by assessment of QoL. As indicated in Study III, it cannot be concluded from analyses performed in this project whether the QoL for this ASD study population is comparable with the QoL of the general population. Since the QoL scale administered, i.e. the INICO-FEAPS Scale, is adapted to individuals with intellectual and/or developmental disabilities, it is apparently not directly applicable for administration to the general population. However, several reviews and a meta-analysis conclude that individuals with ASD, in general, have lower levels of QoL than typically developing individuals (Ayres et al., 2017; Chiang & Wineman, 2014; Ikeda et al., 2014; Van Heijst & Geurts, 2015).

As discussed in Study III, the lowest mean scores for both self-reports and parental proxy-reports were found for the domains emotional well-being and interpersonal relationships. Consistent with these results, low scores for similar domains – The World Health Organization Quality of life (WHOQOL)-BREF (The WHOQOL Group, 1998) domains of psychological health and social relationships – were found in other studies investigating QoL in adults with ASD (Hong et al., 2016; KampBecker, Schroder, Remschmidt, & Bachmann, 2010; Lin, 2014). Several explanations might account for these findings. The generally high prevalence of depression found in individuals with ASD (Wigham, Barton, Parr, & Rodgers, 2017) might impact on the low mean scores found for domains related to emotional well-being and psychological health. Moreover, as found in Study III, the presence of psychiatric comorbidity, in general, and also sleeping difficulty and maladaptive behavior, was found to be associated with a lower level of QoL: the presence of one or more of these factors may influence the overall emotional well-being, resulting in a low mean score for this domain in INICO-FEAPS. The low mean scores found for the domain of interpersonal relationships might be a reflection of the core difficulties of individuals with ASD, including deviant reciprocal social interaction and communication. Difficulties with functioning in the social world are often reported by adults with ASD, along with loneliness and harassment (Mazurek, 2014; Milovanov, Paquette-Smith, Lunsky, & Weiss, 2013; Pfeiffer, 2017).

Interestingly, results for self-reports and matched parental proxy reports differed significantly for the domain of interpersonal relationships with a higher mean score for self-reports. This indicated that even though the rating for self-reports in this domain was among the lowest rated, the individuals with ASD were generally more satisfied with their interpersonal relationships than what their parents thought. The significant difference found for this domain might derive from a qualitative or quantitative difference with regard to extent of social needs. Even though the parents were asked to rate the QoL of their son or daughter, as they thought he or she would do themselves, the social needs of an individual with ASD might be difficult to grasp fully. However, overall the results emphasized that support and intervention directed at emotional well-being and interpersonal relationships might not be adequate for this population, and to improve QoL these must continue to be areas of future intervention.

In studies III and IV, the results of QoL and daytime activity were combined, and comparisons of daytime activity groups on QoL were further provided in this thesis (Table 6). In general, QoL was associated with having a current daytime activity in terms of being enrolled in education or engaged in occupation: individuals without a regular daytime activity were found to have a lower QoL (Study III). Similarly, for 18–26 year olds, the group without a regular daytime activity had a lower QoL than groups engaged in different occupations or education. Even though the group of individuals with normative education/occupation were found to have the highest QoL, the group in customized education/occupation still had a higher mean level of QoL than the group without a regular daytime activity. As stated in Study IV, several studies have emphasized the importance of having a daytime activity (García-Villamisar & Hughes, 2007; Hendricks, 2010; Holwerda, van der Klink, de Boer, Groothoff, & Brouwer, 2013; Taylor, Smith, & Mailick, 2014), including studies of the opinions of adults with ASD themselves (Baldwin et al., 2014). However, the same group of adults with ASD also mention negative aspects of being employed in terms of it, for example, being repetitive, boring, or unfulfilling work, or when there is a lack of adequate instruction, training, or support (Baldwin et al., 2014). This illustrated the importance of having an appropriate daytime activity with adequate considerations and support, if necessary. In this PhD project, the young adults employed were generally satisfied, according to parental evaluations, with their occupation in terms of, for example, experience of success, and match between occupation and educational level (Study IV, Table 2). Even though this evaluation was based on parental ratings, this might explain, in part, the positive association found between QoL and daytime activity. However, a parallel explanation cannot be drawn with regard to satisfaction with eventual current enrollment in education, since the survey did not contain any items on that topic.

5.2. ASSESSMENT OF QUALITY OF LIFE IN THE SURVEY AND IN ASD POPULATIONS IN GENERAL

Several methods for the assessment of QoL exist with varying usability according to age groups, different modes of administration (i.e., interview, self-administered rating scale), and reporting (i.e., self-reports, proxy reports). In addition, some QoL assessment methods are generic and some are specific for different groups of disability or diseases. For individuals with ASD, no specific method for assessment of QoL was available for self-report prior to launch of the survey. For proxy reporting, Billstedt et al. (2011) presented QoL measures named "autism-friendly environment" and "parent/carer-rating of individual's well-being," intended for assessment of QoL in an ASD study population, where the majority had severe learning disabilities. Overall, as illustrated in a recent review, as well as in recent studies of QoL in adults with ASD, the WHOQOL-BREF scale (The WHOQOL Group, 1998) is one of the most frequently applied scales for assessment via self-report (Ayres et al., 2017; Bishop-Fitzpatrick, Mazefsky, & Eack, 2017; Hong et al., 2016; Moss et al., 2017). However, the WHOQOL-BREF is usable for self-administration, if the individuals have the ability to do this; otherwise, assistance is recommended in terms of carrying out an interview (World Health Organization, 1996). Whether individuals with ASD have the ability to complete the WHOQOL-BREF scale might be evaluated by researchers with knowledge of the characteristic of the sample in question. As found in several studies investigating self-reported QoL in adolescents and adults with ASD, inclusion criteria for the study participants were an IQ at least above the level for ID (i.e., IQ>70) (Bishop-Fitzpatrick et al., 2017; KampBecker et al., 2010; Lin, 2014). Further, as reported by Hong et al. (2016), who included individuals with ASD both with and without ID in their study sample, the WHOQOL-BREF scale was administered as an interview but modified to adjust it to the study population, for example by supplementing text to facilitate the understanding of the items. Like this, different adaptations were made, either to the study population or to the scale. However, when excluding individuals with ASD and ID, results of the studies in question might not be applicable for this particular subgroup of individuals with ASD.

Information on the invited individuals with ASD was not available prior to launch of the survey, including information on, for example, intellectual levels or language abilities. In the event the invited sample consisted of individuals with high proportions of ID and/or language disabilities, reporting on QoL via a generic self-administered scale might have been too difficult for a large proportion of the invited cohort. For that reason, a QoL scale customized for adolescents and adults with intellectual and/or developmental disabilities was chosen in this survey, namely the INICO-FEAPS Scale (Gomez et al., 2015). In addition, the INICO-FEAPS Scale had the advantage of featuring two versions, specifically a self-report form and a report to be completed by another person, who knows the person well (i.e., report of others form). In this way, two adaptations were made for QoL assessment to ensure as many completed QoL ratings as possible. First, a customized scale was applied with the aim of enabling as

many individuals with ASD to self-report on their QoL. Second, in the event individuals with ASD were not able or willing to self-report, their parents had the chance to report as proxies.

Further, the INICO-FEAPS Scale is based on thorough theoretical considerations by building on the theoretical QoL model developed by Robert L. Schalock and Miguel Á. Verdugo (Schalock & Verdugo, 2002; Schalock, Verdugo, Gomez, & Reinders, 2016). According to this model, QoL is multidimensional and features eight domains (corresponding to the eight domains in INICO-FEAPS). The importance of the eight domains has been validated transculturally in several studies (Gomez, Verdugo, Arias, & Arias, 2011; Jenaro et al., 2005; Schalock et al., 2005; Wang, Schalock, Verdugo, & Jenaro, 2010). Hence, the INICO-FEAPS Scale was tailored to the method for this survey according to the age group of participants, a study population including individuals with intellectual and/or developmental disabilities, and the need for both a self-report form and a proxy report form of the scale, in addition to the advantage of being based on a well-investigated and comprehensive theoretical framework.

The importance of establishing the psychometric properties of a QoL scale applied in an ASD sample was emphasized by Ikeda et al. (2014), and the reason for carrying out Study II. Thus, it was important to investigate whether the INICO-FEAPS Scale had comparable psychometric properties to the original paper of validation (Gomez et al., 2015) when administered to an ASD population. According to the results presented in Study II, overall acceptable results were found for the psychometric properties investigated, including an acceptable fit to the predefined model with eight correlated first-order factors. Recently, dimensionality and internal structure of the Colombian version of the INICO-FEAPS Scale was investigated for a sample of adults with ID (Verdugo-Alonso, Henao-Lema, Córdoba-Andrade, & Arias González, 2017). As was the case in the original validation paper (Gomez et al., 2015), the eight-factor model continued to show the best fit to data. Furthermore, another instrument based on the eight-factor model of QoL of Schalock and Verdugo, the KidsLife Scale, was investigated using a sample of children with ASD and ID, again finding support for the eight-factor structure (Arias et al., 2017). Overall, these findings, including the findings of Study II, indicate that the eight separate domains seem to be important for understanding the construct of QoL for individuals with ID, as well as those with ASD. These findings also indicate the multidimensionality of QoL, in other words that different domains contribute to QoL.

As presented in Study I, only a minority of the study population of this project had ID and language disabilities. The implications of this finding in relation to the administration of INICO-FEAPS can be discussed. For example, it is possible that the individuals with the highest level of functioning in this sample found the content of at least some items irrelevant to their current situation. Some items took a need for support as a starting point, which does not appeal to a responder without this need for support. This might have resulted in making the INICO-FEAPS Scale less user-

friendly for a subgroup of the study population, which might have caused irritation, interruption of completion of the scale, a higher degree of missing items, or simply odd answering. However, modifications of some of the items were made prior to launch of the survey for easing answering of the items, whatever the functioning of the individual (Study II). Furthermore, the QoL model of Schalock and Verdugo is not limited to the field of intellectual and developmental disabilities (van Hecke et al., 2017). Hence, the domains of the INICO-FEAPS Scale are of relevance whatever the level of functioning.

Even though the theoretical model of QoL developed by Schalock and Verdugo has been thoroughly investigated, applied theoretically to the ASD population (Plimley, 2007), and a comprehensive statistical investigation of the psychometric properties was conducted with acceptable results obtained (Study II), it could have been relevant prior to the administration of the INICO-FEAPS Scale in the survey to apply a qualitative approach using the same scale with the purpose of receiving feedback on the scale from adolescents and adults with ASD. First, in order to see how the participants interpreted the items; and, second, the qualitative information provided by the individuals with ASD could have improved interpretation of results. This includes, for example, reasons for scoring low or high on the different domains in the INICO-FEAPS Scale. Lastly, in order to assess the ecological validity when it comes to investigating QoL in an ASD study population. It is currently unknown whether the INICO-FEAPS Scale lacks topics of high relevance for QoL for individuals with ASD. For example, in general, the domains of INICO-FEAPS might be relevant to QoL for adolescents and adults with ASD overall; however, when the domains are operationalized as specific items, the exact content might not be adequate and thus not valid. Yet, as emphasized by Burgess and Gutstein (2007), it is a challenge in QoL research to develop assessment tools that capture the most predictive indicators for the population in question.

Interpretation of the items in QoL scales have been investigated to some degree. For typically developing children, Davis et al. (2007) investigated the discordance between child self-reported and parent proxy reported health-related QoL via qualitative methods with 15 parent–child pairs. They concluded that the discordance may be a result of a difference in reasoning and different response styles rather than interpretation of items. For example, children had a tendency to rate items with more extreme scores. However, Tavernor, Barron, Rodgers and McConachie (2013) demonstrated in a small sample (n=11) that misinterpretation of items in QoL scales happened for some children with ASD, who, for example, had a literal understanding of some items. It is unknown, whether this also applies to adolescents and adults with ASD, and specifically whether the self-reporting individuals in this study understood the items as intended. According to the analyses performed, results from the self-report differed compared with matched proxy reports (Study III). This is not, however, interpreted as misunderstandings of content of items but rather that self-reported QoL is found to differ compared with proxy reports, both among individuals with ASD and

typically developing individuals (Clark, Magill-Evans, & Koning, 2015; Egilson, Ólafsdóttir, Leósdóttir, & Saemundsen, 2017; Ellert, Ravens-Sieberer, Erhart, & Kurth, 2011; Hong et al., 2016; Sheldrick et al., 2012; Stokes, Kornienko, Scheeren, Koot, & Begeer, 2017). Hence, self-reported and proxy reported QoL are considered to be two different sources of information; however, it should be emphasized that QoL is subjective, and that self-reported QoL is preferred to gain insight into the QoL of people with ASD (Verdugo, Schalock, Keith, & Stancliffe, 2005).

The need to develop valid measures for assessment of QoL of individuals with ASD has also been emphasized by several researchers (Ayres et al., 2017; Burgess & Gutstein, 2007; Moss et al., 2017), referring to the issue of whether applied QoL scales include all relevant topics for individuals with ASD. Some researchers have suggested QoL scales specific for individuals with ASD (Plimley, 2007; Tavernor, Barron, Rodgers, & Mcconachie, 2013). Yet another possibility is to adapt existing QoL scales for the ASD population (Ayres et al., 2017). Recently, a research group from Newcastle University, UK, has published work on the development of additional items to add to the WHOQOL-BREF with the purpose of making the assessment of QoL reliable and valid for adults with ASD, while maintaining the possibility of comparing it with the general population (Mcconachie et al., 2017). A total of nine items were added, covering topics such as support, sensory issues, and "autism" as an aspect of identity, and the process included active involvement of adults with ASD (Mcconachie et al., 2017). Thus, the WHOQOL-BREF including the ASD specific items is the first QoL scale for self-report specifically for adults with ASD. However, as stated in Ayres et al. (2017), more than one QoL scale for individuals with ASD may be needed, for example differing for individuals with and without ID. This point is central and can be part of the solution of measuring QoL in as heterogeneous a population as individuals with ASD.

5.3. VALIDITY OF ASD DIAGNOSES OF THE STUDY PARTICIPANTS

Participants in the present study were identified via the DPCRR according to the inclusion criteria mentioned in the methods section. ASD diagnoses were given several years prior to participation in the survey by clinicians at Danish child psychiatric hospitals applying the ICD diagnoses available in Denmark at the time (i.e., ICD-8 or ICD-10). Owing to the year of birth (i.e., 1990–1999) of the invited participants, combined with the relatively high mean age at diagnosis of ASD (9.22 years), and the fact that ICD-10 was implemented as of 1994 (Mors et al., 2011), the large majority of participants in this cohort were diagnosed according to ICD-10 criteria for ASD (World Health Organization, 1992). In general, child psychiatric assessments in Denmark are performed with different disciplines working together to obtain the most appropriate diagnosis to describe the difficulties for the specific child.

However, for the study population in this survey, the exact methods and assessment procedures used for diagnosing ASD are unknown, and confirmation of each of the ASD diagnoses given cannot be obtained. However, a study validating the diagnoses of infantile autism in the DPCRR has been conducted. In this study, the patient files of 499 children born in the period 1990–1999 were reviewed and the diagnoses were confirmed for 94% of the sample (n=469); however, only five cases were classified as non-ASD (Lauritsen et al., 2010). In the same study, a small sample (n=39) with ICD-10 autism diagnoses other than infantile autism were selected, patient files were reviewed, and only four cases were classified as non-ASD. Therefore, the registration of the diagnosis of, in particular, infantile autism in DPCRR can be considered to be valid. It should be noticed that an overlap in selected participants for this study (n=6218), and the participants with a validated ICD-10 autism diagnosis in the DPCRR (n=521), can occur, although the actual overlap for responding participants is unknown.

Although the ASD diagnoses of the adolescents and adults in the current study population were not clinically confirmed at the start of the study – for example with the often-used assessment methods of the Autism Diagnostic Observation Schedule, second edition (ADOS-2) (Lord et al., 2012) and/or the Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994) – information was available, which makes it plausible that the individuals were diagnosed with ASD in childhood and that this diagnosis was and maybe still is characterizing the difficulties of the individuals invited to participate in the study. First, it was very clear in the invitation to participate in the survey that this study dealt with outcomes for individuals diagnosed with ASD in childhood, making it unlikely that parents and/or the individuals with ASD completed it if this topic – for various reasons – was irrelevant to them. However, in the event that an incorrect diagnosis of ASD was given in childhood, but the family was persuaded that the diagnosis was correct, they might still have completed the questionnaire. It should also be noted that the similarity between the ICD-10 autism diagnoses reported by the parents and the ones drawn from the DPCRR is considerable (Study I). However, this comparison was only possible on a group level and not on a one-to-one comparison, indicating only a possible high degree of agreement. However, overall, it is reasonable to assume that the study population in this survey received an ICD-10 autism diagnosis from professionals at Danish child psychiatric hospitals of relevance to the families, who thereby chose to participate in the survey.

The RAADS-14 Screen was filled out for 1465 individuals with ASD, and a mean total score of 24.46 (SD=0.26) was found. As suggested by Eriksson, Andersen and Bejerot (2013), a cut-off of 14 provided the best discrimination of individuals with or without ASD, resulting in a sensitivity of 0.97. This may suggest that these individuals, in general, can still be considered to have ASD. By dividing the study population into subgroups of QoL respondent types (Study III, Table 4) or according to daytime activity (Study IV, Table 3), similar mean RAADS-14 Screen scores were

obtained but with a lower score for the subgroup with a normative occupation or in education (RAADS-14 Screen total mean score=19.82). The RAADS-14 Screen is not, however, a diagnostic tool but constructed as a screening tool. Hence, it is important that the RAADS-14 Screen score is used as in indicator of the existence of ASD symptoms only, not for confirmation or disconfirmation of the diagnosis of ASD. Individuals participating in the current study with a RAADS-14 Screen score below the cut-off exist, and it can be questioned whether they still have ASD or whether the RAADS-14 Screen is not sensitive enough to capture the symptoms. It should also be taken into account that the suggested cut-off score is based on a self-report of RAADS-14 Screen and not parental report, as applied in this project. Even though the RAADS-14 Screen has been piloted with parents reporting instead of individuals with ASD themselves (J.M. Eriksson, personal communication, May 16, 2015), the exact implications of change of respondent type are not known. However, in a study by Bishop and Seltzer (2012), self-reports on ASD symptoms tended to be lower than parental reports, which was considered to be due to unawareness of own social behavior according to the perspective of others. This study did not, however, apply the RAADS-14 Screen, but it is important to take into consideration that the cut-off score in the RAADS-14 Screen is estimated from self-reports, and if differences in ratings exists for self- and parental reports, this might also affect the cut-off.

Differences between the sample used for validation of the RAADS-14 Screen and for this PhD project should also be considered as important for the level of ASD symptom rating. This issue, in general, has also been addressed by Bishop and Seltzer (2012). Whereas the study population used for validation of the RAADS-14 Screen (Eriksson et al., 2013) was primarily recruited from psychiatric clinical settings, the study population in the current project was population-based and diagnosed years ago. Hence, the families in this project may no longer focus to the same degree on the difficulties caused by ASD, or may evaluate the symptoms as less severe owing to improvement or acclimatization over the years. Overall, the RAADS-14 Screen scores found for the present study population indicate the presence of ASD; however, as discussed several considerations should be taken into account and no firm conclusion can be drawn on the basis of the results of RAADS-14 Screen alone.

In general, diagnostic stability has been investigated in several studies. Howlin et al. (2013) carried out a long-term follow-up study of children diagnosed with ASD in childhood at a mean age of 6 years (n=60). Subsequently, diagnostic reconfirmation was performed using the Autism Diagnostic Interview (ADI) (Le Couteur et al., 1989), and 88% of the study participants met the cut-off for the three core domains of ADI; the remaining 12% met the cut-off for two domains. At follow-up (mean age 44 years; n=58), 45% met the cut-off for the three core domains of ADI-R (Lord et al., 1994) and 55% met cut-off for two domains. As suggested by Howlin et al. (2013), all individuals continued to meet the diagnostic criteria for ASD on the ADI-R, but the severity of ASD symptoms declined from childhood to mid-adulthood. However,

the sample used in Howlin et al. (2013) was diagnosed at a time when presumably only children with the most severe symptoms of ASD were diagnosed. Accordingly, these results cannot be directly compared with the study population of the current project. Yet, for individuals with Asperger's syndrome diagnosed in childhood, Helles, Gillberg, Gillberg and Billstedt (2015) investigated stability of the diagnosis over an average of 19 years, with the latest assessment when the participants were a mean age of 30 years. When the initial diagnosis of these adults (n=47) were evaluated according to any ASD diagnosis applying DSM-IV criteria, they found a decrease in individuals fulfilling an ASD diagnosis from 91% at first follow-up to 76% at second follow-up. As stated in Lord, Bishop and Anderson (2015), ASD symptoms are not static within individuals across development. In their study, following a sample diagnosed with ASD in early childhood until early adulthood (n=85), a decrease in ASD symptoms was found, not only for repetitive behavior, but also for social and communicative difficulties. This sample consisted of individuals who in adulthood were found to have heterogeneous outcomes in terms of functioning and intelligence.

By applying this knowledge to the study population in this project, a decrease in autism symptoms from the time of diagnosis of ASD to the time of the survey might be expected, independent of the initial severity of autism symptoms. However, for the subgroup of individuals diagnosed with Asperger's syndrome, which constituted about 40% of this sample, the decrease in autism symptoms might be to such an extent that some of them no longer meet the diagnostic criteria for ASD, as indicated by the range of the RAADS-14 Screen total score (section 4.2.). The same might be the case for the study participants with the ICD-10 diagnosis Other PDD, as indicated by Rondeau et al. (2011), even though this meta-analysis only investigated diagnostic stability in childhood. However, it is important to distinguish between the validity of the first-time diagnosis of ASD and the validity of a current diagnosis of ASD. As stated, it is reasonable to assume that the ASD diagnoses applied to the individuals with ASD in this survey by professionals at psychiatric hospitals for children in Denmark are acknowledged by the families, who chose to complete the survey. When it comes to whether the individuals currently meet the diagnostic criteria for ASD, no clear answers can be given. Cases of so-called optimal outcomes in terms of, for example, having a low level of autism symptoms are documented, and it is estimated that 3–25% of children diagnosed with ASD will not meet the diagnostic criteria for ASD when growing up; however, criteria for optimal outcomes have not yet been refined (Kaboski et al., 2017). It is unknown whether a subgroup of individuals in the present study population can be defined as having optimal outcomes. Nevertheless, it should also be emphasized that this study sample was primarily diagnosed according to ICD-10 criteria, which for some diagnoses include individuals with a small degree of autism symptomatology compared with DSM-5 (Helles et al., 2015), and apparently ICD-11 as well. Thus, for this study population a higher proportion of possible optimal outcomes might be expected compared with both future outcomes for children diagnosed according to DSM-5 or ICD-11 and also compared with previous follow-up studies including individuals diagnosed in the past with an autistic

disorder (e.g., Howlin et al., 2004). As stated by Barahona-Corrêa (2017), reflecting on the varying diagnostic criteria for ASD over time: “it is not always clear whether patients have outgrown the disorder or whether diagnostic criteria have outgrown the patients” (p. 159). This condition seems inevitable when performing ASD outcome research, highlighting the need to address the possible implications of using a particular study sample.

5.4. CHOICE OF ASSESSMENT TOOLS AND VALIDITY OF SURVEY DATA

In a recent review covering outcomes in adulthood for individuals with ASD, Howlin and Magiati (2017) emphasized the need for systematic research stating that the variability in measures used might be a part of the explanation of inconsistent and even contradictory results found when investigating this topic. Across studies there seems to be no consensus regarding measurement tools used for assessment of outcome, although this is the case when choosing measurement tools for investigation of some topics, for example the application of the WHOQOL-BREF scale (The WHOQOL Group, 1998) for assessment of QoL in adolescents and adults with ASD, and the use of ADOS-2 (Lord et al., 2012) and/or ADI-R (Lord et al., 1994) for assessment of ASD symptoms.

In this PhD project, it was a challenge to determine which tools to use for assessment of the subjects of interest. Preferably, the scales should be able to be used for self-administration, to measure the topics of interest with high validity, to be standardized in Denmark, and to be standardized for, or at least tested with, the right informant group (i.e., parental or self-report). Furthermore, scales intended for individuals with ASD, or generic scales previously applied in an ASD population, were preferred. However, not all of these requirements could be met for the assessment tools administered in the survey. Furthermore, legal considerations should be taken into account: in case a scale is formally published, permission should be obtained from the publisher to administer it in an online version. Finally, it was necessary to take into consideration the total length of the questionnaire in both the self-report form and the parental form of the survey. For the self-report form the aim was to facilitate as large a group of individuals with ASD to complete the questionnaire as possible, making it of high importance to provide a manageable questionnaire. Owing to the aim of this project, including evaluating outcome on several parameters, the parental version of the questionnaire needed to be more comprehensive but not too exhaustive to complete. For one of the main outcome parameters, QoL, the primary tool for measurement was the INICO-FEAPS Scale, as previously addressed (section 5.2.). Further, inclusion of a comprehensive measurement of adaptive functioning was prioritized, which resulted in the choice of ABAS-II owing to the fact that it is widely used in Denmark for the assessment of adaptive behavior in adolescents/adults with

ASD. However, the ABAS-II has not been validated in a Danish sample and there are no Danish norms available. Nevertheless, no scale assessing adaptive behavior currently provides Danish norms up to the age of 26 years, which is the upper age limit of participants included in this study.

Some topics in the survey, for example presence of ID, maladaptive behavior, and psychiatric comorbidity, were covered via questions created for this survey specifically. However, this approach may not be without implications for the results obtained. Certainly, presence of ID should be assessed using a standardized test of intelligence, such as the Wechsler Adult Intelligence Scale – fourth edition (WAIS-IV) (Wechsler, 2008). It is a possibility that parents are reluctant to report information on ID because having a child with ID may be associated with a degree of shame. If this is the case for the present survey, the rate of ID found is underestimated. However, for subgroups of the study population classified according to daytime activity, the proportion of ID and overall level of adaptive functioning according to ABAS-II (GAC score) is provided (Study IV, Tables 3 and 4), and these two estimates, in general, followed the same trend. Like that, a low proportion of ID is accompanied by a higher GAC score and the other way around. These results suggest valid reporting of ID.

Parental report of maladaptive behavior and psychiatric comorbidity have been used in previous studies of adolescents and adults with ASD (Bishop-Fitzpatrick et al., 2016; Eaves & Ho, 2008; Farley et al., 2009; Ruble & Dalrymple, 1996; Taylor & Henninger, 2015). Similarly, in this survey the presence of maladaptive behavior was assessed without administering a scale, only by questions directed to the parents. Even though examples of different types of maladaptive behavior were provided, as well as the instruction to only mark the type of maladaptive behavior as present if the behavior resulted in problems in everyday life for the individual with ASD and/or his or her surroundings (Study III and Study IV), it would still have been preferable to apply a standardized scale, and several scales exist for assessment of, for example, maladaptive behavior and related issues (Matson & Cervantes, 2014). However, at the time of planning and conduction of the survey, it was not possible to locate an available scale that matched the responders (parents to 16–26 year olds) and that was able to be administered in an online survey. For psychiatric comorbidity, the validity of the results in this project is dependent on whether the parents understood the content of the psychiatric diagnoses suggested, whether they knew what psychiatric diagnoses their child had, and/or whether they wanted to disclose the psychiatric diagnoses of their child. Some studies on psychiatric comorbidity in ASD have used telephone interviews of parents about the psychiatric comorbidities of their adult child with ASD (Eaves & Ho, 2008; Farley et al., 2009), enabling the interviewer to explain, if there was any doubt. However, some parents might be more reluctant to disclose psychiatric comorbidity over the telephone compared with in a survey. Because parents to adult children with ASD usually continue to be very involved in the lives of their children (Howlin et al., 2013), the parents might also be informed about presence of psychiatric

comorbidity. However, the questions in the survey assumed that the individual with ASD had undergone professional assessment for psychiatric comorbidity, as the parents were asked whether their child was diagnosed with one or more psychiatric diagnoses. Accordingly, unobserved and/or undiagnosed comorbidities may not be marked. For that reason direct assessment of psychiatric comorbidity of the study participants would have been preferable, but it was difficult to accomplish in a survey-based project. Nevertheless, this may, in part, explain the relative low rates of psychiatric comorbidity found in this survey. Obviously, another reason for the low rates found is the use of a population-based sample versus a sample of psychiatry-referred individuals, who will show more frequent psychiatric problems. As stated by Moss, Howlin, Savage, Bolton and Rutter (2015), there seems to be no consistency in overall rates of psychiatric comorbidity, yet a higher degree of consistency is found for the most frequent types of psychiatric diagnoses associated with ASD. Indeed, as discussed in Study I, the most frequent psychiatric diagnoses found for the study population in this project match the most frequent types found in other studies, which might increase the likelihood that parents reported correctly. It should be mentioned that assessment of psychiatric comorbidity in adults with ASD is further complicated by the lack of validated measures for assessment of mental health for this population; hence, the presentation of psychiatric problems for adults with ASD is often atypical (Moss et al., 2015). For example, anhedonia might be expressed as a reduction in the time used in activities previously considered as obsessive by others, which can be misinterpreted as improvement in ASD behavior (Filipe, 2017).

For ASD symptoms, the RAADS-14 Screen (Eriksson et al., 2013), developed for self-reporting, was applied to parental report. Obviously, even though parental reporting on RAADS-14 Screen had been piloted (J.M. Eriksson, personal communication, May 16, 2015), a self-administered scale intended for parental report would have been more appropriate. Questionnaires such as the Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2003) or Social Responsiveness Scale (SRS) (Constantino & Gruber, 2012) could have been applied instead; however, these scales hold a considerably higher number of items when taking the total length of the parental questionnaire into consideration. Nevertheless, the purpose of assessment of ASD symptoms in this survey was not to get current confirmation of the ASD diagnosis but rather to get an estimate of the number of current symptoms, whether or not the study participants still fulfilled the diagnostic criteria for ASD. Hence, for current confirmation of the ASD diagnosis clinical assessment with a standardized tool according to the diagnostic system used is necessary. Above all, the total score of the RAADS-14 Screen was mainly applied in regression analyses as a continuous variable, and the proposed cut-off score used for screening for ASD has only been sparsely used and interpreted with caution.

In conclusion, clinical assessment of psychiatric comorbidity and ASD symptoms with a standardized tool, and formal testing of intelligence would have been preferable in order to secure a more valid and comprehensive assessment. Furthermore, results

from clinical assessment are usually thorough, providing a high degree of detail applicable to further analyses, such as domain sub-scores. However, for this survey clinical assessment of each person would have limited the sample size considerably, and, in general, have changed the overall methodology from a survey to a clinical study. Bias in survey data will occur, for example due to misinterpretations of questions asked. Yet, instructions on how to answer the questions asked were provided in plain language, and the parents and adolescent/adult with ASD could access help via e-mail or telephone if further support was needed. In general, the assessment tools applied and the questions prepared specifically for this survey were inspired by those used in other studies (cf., section 3.4.) with the aim of building upon the experience of these other studies. Hence, the advantage of this survey and the methodology applied was the possibility of collecting data systematically for a large sample of individuals with ASD.

5.5. REPRESENTATIVENESS OF THE SURVEY RESPONDENTS

The individuals with ASD were identified via DPCRR, yielding a nationwide and population-based sample of individuals diagnosed with a diagnosis of ASD. Assessment and treatment in public Danish hospitals, including psychiatric hospitals for children and adolescents, is free of charge, and a diagnosis is often preferred prior to establishing support and services to the child with ASD and the family as a whole. This supports the possibility of sampling a representative study population, thereby minimizing the impact of selection bias, which is often found in studies of individuals with ASD. For example, selection of study participants was estimated as a risk of bias in 35 of 45 studies evaluated in a systematic review of measurement properties of screening and diagnostic tools for adults with ASD (Baghdadli, Russet, & Mottron, 2017). However, when conducting a survey the risk of selection bias should be investigated, because not every invited family chooses to participate in the survey. Thus, comparing responders and non-responders is of high importance.

In Study I, the representativeness of responders and non-responders was evaluated by comparing them on sociodemographic and psychiatric factors. Because the invitation to participate for both parents and the individual with ASD were sent to the parents, responder status was defined according to parental response. Hence, it was the choice of the parents to distribute the invitation to their child or not. Owing to the inclusion of both completed and partially completed questionnaires, the actual group of responders differs slightly across analyses conducted in studies I–IV. Therefore, it could be argued that the results of the analyses comparing responders and non-responders do not apply directly to all studies included in this project. In addition, sophisticated approaches for conducting analyses comparing subgroups of responders and non-responders exist, for example by analyzing significant attrition points during the survey for individuals, who started to respond, and characteristics of individuals

who drop out at these points and overall (Hochheimer et al., 2016). However, the choice of applying the more simple approach was pragmatic in terms of leaving room for analyses of outcome for adolescents and adults with ASD. Instead, a broad range of variables was chosen to enable a thorough comparison of responders and non-responders on several parameters according to psychiatric history and sociodemographics.

The overall response rate might be of concern when the extent of representativeness is estimated, and therefore might be a source of bias in the results of this survey. In general, response rates for web surveys have been found to vary considerably, from 12% to 67% (Shin, Johnson, & Rao, 2012). For surveys involving individuals with ASD and their families, several studies did not report response rate(s) (Crane, Chester, Goddard, Henry, & Hill, 2016; Jones, Goddard, Hill, Henry, & Crane, 2014; Khanna, Jariwala, & West-Strum, 2015; Parsons, 2015). For surveys involving parents of children with ASD, response rates of 28–29% were found (Kalb, Cohen, Lehmann, & Law, 2012; Kamio et al., 2013). Higher response rates were found in a survey of adults with ASD (40%; n=102/255) and legal guardians of adults with ASD (42%; n=60/255) (Gotham et al., 2015). However, these rates were calculated from a second wave of follow-up, and no response rate was available for the first wave of the survey conducted. Comparing the response rate of this survey to other studies using survey methodology, the finding can be assumed as acceptable. First, the response rate of the parents in this survey is not lower than in surveys of parents of children with ASD. Second, this survey had, in contrast to many other surveys, the advantage of having access to data, making calculation of response rate possible, and even more importantly making comparisons of responders and non-responders possible. As discussed in a Danish paper, the motivation for participation in online surveys may have declined over time in Scandinavian countries, and further the fact that the invitation to participate in the survey was posted from a psychiatric research unit might have resulted in a lower response rate owing to prejudice associated with mental health organizations (Carrozzino et al., 2016).

The higher response rate among parents versus individuals with ASD is not surprising, as a subgroup of invited individuals with ASD potentially would not be able to complete the self-report questionnaire owing to severity of ASD and ID. Furthermore, parents had the responsibility of distributing the invitation to their child, which may not have happened for several reasons. As mentioned previously, a single reminder was sent out, which presumably has resulted in a higher response rate. Owing to time constraints, it was not possible to mail another reminder. Additional initiatives for improving the response rate, for example combining multiple e-mail and postal contacts (Millar & Dillman, 2011), were not possible. Parental addresses were provided by the Danish Health Data Authority, but not personal registration numbers, which could have been used to e-mail invitations to the Danish personal digital mailbox (“e-Boks”) also used by public authorities.

According to the analyses presented comparing responders and non-responders there were only few significant differences with at least a small effect size: distribution of ICD-10 autism diagnoses, parental residence according to the Danish geographic regions, parental educational level, and parental main occupation according to income for the individual responder and household of responder. However, owing to small differences in actual proportions for the first two parameters, as presented in Study I, the most important differences were found for parental educational level and parental main occupation. This means that parental responders of the survey tended to have accomplished a higher educational level compared with non-responders and, to a higher extent, be in the labor market. As discussed in Study I, there might be a general tendency for individuals participating in research to be more socioeconomically advantaged than individuals who do not participate (Egilson et al., 2017; Rodriguez, Tuvemo, & Hansson, 2006). This tendency introduces non-response bias, which can affect the results presented. For example, the included individuals with ASD might come from families with a higher extent of available resources to support them, which might improve their outcome in terms of better adjustment in adolescence/adulthood (Marriage et al., 2009). Reduction of the total length of the parental questionnaire and/or to allow completion of the questionnaire over the telephone might have resulted in inclusion of higher proportions of socially disadvantaged families. However, these methods might have other shortcomings, for example the perception of pervasiveness of some families.

Furthermore, it can be argued that the low rates of, for example, psychiatric comorbidity compared with other studies, as presented in Study I, might at least partly derive from a non-representative sample. Following this line of reasoning, it is possible that families where the individual with ASD suffers from a psychiatric comorbidity had less time and resources available to comprehensively complete a questionnaire. This assumption was partly supported by the feedback provided by a small subgroup of non-responders to the survey, who reported that they did not have the resources, at least currently, to complete the survey (section 4.1.). Parenting for children with ASD, including when they grow up, is challenging and demanding (Ludlow, Skelly, & Rohleder, 2012; Washington Barnes, 2015), and in families where the individual with ASD is also affected by other disabilities, the resources of the parents might at least periodically be few, resulting in refusal to participate in research. However, the tendency to include more socioeconomically advantaged and resourceful families or individuals in research might be difficult to obviate in carrying out research.

When placing the results in an international context, the frequencies of the different ICD-10 autism diagnoses in this study population should be considered. For example, the proportion of individuals with Asperger's syndrome in the study population appeared large (around 40%); however, it is the most frequent diagnosis for the defined cohort invited, as shown in Study I (Table 5), but differences between countries might exist. In a study comparing ASD prevalence in Denmark and Western

Australia, the diagnosis of childhood autism was found to be more prevalent in Western Australia (39.3 per 10,000) than in Denmark (21.8 per 10,000) but with a higher overall prevalence of ASD in Denmark (68.5 per 10,000) than in Western Australia (51.0 per 10,000) (Parner et al., 2011). The study included children born between 1994 and 1999 with an ASD diagnosis in 2004 at the latest. Thus, the span of year of birth of the included individuals was narrower, and the length of follow-up shorter than definitions made for this project, and therefore the prevalence rates are not directly comparable. Furthermore, it is unknown whether the differences between Denmark and Western Australia have remained over the years. However, in a study by Fombonne (2009), it was estimated from studies published since 2000 that around 30% of all ASD diagnoses relate to infantile autism. Even though this estimation is not based on ICD-10 only, and did not only include individuals diagnosed with ASD in childhood, this estimate for infantile autism is close to what was found in this PhD project. Further, even though it is hard to compare without taking parameters such as length of follow-up into account, the prevalence of ASD found in Danish studies based on DPCRR data and ICD-10 diagnoses (Parner, Schendel, & Thorsen, 2008; Parner et al., 2011) did not differ from what has been reported in general internationally (Elsabbagh et al., 2012; Fombonne, 2009). Accordingly, the potential differences across countries found for proportions of specific ICD-10 autism diagnoses might be due variations in assessing and diagnosing different ASD diagnoses, and not owing to whether the individuals had ASD or not. However, a decrease in ASD diagnoses using DSM-5 criteria versus DSM-IV criteria has been reported (Kulage, Smaldone, & Cohn, 2014). Similarly, a decrease might be found with the implementation of ICD-11, also implying differences between individuals diagnosed with ASD according to ICD-10 versus ICD-11. Therefore, in evaluating the representativeness of this study population the diagnostic criteria used should be taken into account.

Given the overall results of the comparisons of responders and non-responders of this survey, and the method used for identification of potential study participants, the sample of individuals with ASD in this survey are assumed to be highly representative of adolescents and adults diagnosed with a diagnosis of autism in childhood according to ICD-10 criteria.

5.6. STRENGTHS AND LIMITATIONS

Several strength apply to this PhD project, which followed-up children diagnosed with ASD in childhood into adolescence/early adulthood. The sample size was substantially larger than other follow-up studies of children diagnosed with ASD. Furthermore, the sample recruitment method yielded a nationwide and population-based sample, which, to a high extent, was found to be representative of adolescents and young adults diagnosed with an ICD-10 diagnosis of autism in childhood. Additionally, the outcome parameters explored in the survey were comprehensive,

including both objective and subjective perspectives of outcome. Also, the combination of a large sample size and the different measurements of outcome allows for multiple comparisons across subgroups defined according to analysis of interest.

However, several limitations should be taken into account. It was not possible to confirm the ICD-10 diagnoses of autism at the start of the study; additionally, it was not possible to verify the survey data provided by parents. In particular, recall bias might have affected historical information provided by parents. However, difficulties with understanding the questions asked and lack of knowledge about the topic of interest might also have introduced bias to the data provided by parents. The administration of scales solely in the survey would have been preferable; however, this was not possible for every topic investigated. In this regard, there is a scarcity of standardized Danish scales. For the assessment of QoL, the INICO-FEAPS Scale was used; however, whether the content of the items in this scale covered the most essential topics of QoL for individuals with ASD was not examined. Last, a large group of the adolescents and adults with ASD in the study population might have been able and willing to provide further knowledge about themselves in the survey. This would have improved the results involving a more subjective view, for example the string of questions concerning the experience of engagement in occupation (Study IV).

CHAPTER 6. CONCLUSIONS

In this PhD project, outcomes for adolescents and young adults diagnosed with ASD in childhood were investigated using a nationwide and population-based sample and involving different parameters of outcome. Specifically, the project focused on QoL and current daytime activity in addition to a general description of the study population, including psychiatric comorbidity and adaptive functioning.

Initial responders of the survey were compared with non-responders on psychiatric history of the individuals with ASD and sociodemographics of the individuals with ASD, as well as their parents. In these analyses only minor differences were found; however, there was a tendency that more socioeconomically advantaged families to a higher extent completed the survey.

Overall, lower proportions of ID, language difficulties, psychiatric comorbidity, and maladaptive behavior were found than in previous studies, as well as a relatively high mean level of adaptive functioning. This might be attributable to the use of a population-based sample, as well as a sample diagnosed using ICD-10 criteria for autism diagnoses, which includes less severe diagnoses of autism than previously used diagnostic systems.

The INICO-FEAPS Scale was administered for assessment of QoL, and the psychometric properties according to internal consistency, internal structure, and convergent validity were investigated. Overall, acceptable values were found, suggesting that the INICO-FEAPS Scale can be used for assessment of QoL in individuals with ASD. However, whether the scale comprises all topics relevant for QoL in ASD populations has not been explored. Results from the INICO-FEAPS Scale support earlier findings that proxy reports of QoL cannot validly replace self-reports. Furthermore, low scores in the INICO-FEAPS were found for the domains of interpersonal relationships and emotional well-being. Factors such as psychiatric comorbidity, sleeping difficulty, ID, maladaptive behavior, adaptive functioning, autism symptomatology, main daytime activity, and residence were associated with QoL, independent of informant group (i.e., proxy or self-reports), but the importance of each factor for QoL varied, suggesting individual differences within the sample.

For the young adults in the study population, type of current daytime activity was investigated. About one-fifth of the sample did not have any regular daytime activity. The remainder of the study population was engaged in different types of so-called normative or customized education or occupation. Compared with other groups of daytime activity, the group in normative education/occupation had the lowest proportions of ID, maladaptive behavior, psychiatric comorbidity, the lowest level of autistic symptoms, and the highest level of adaptive functioning and QoL. The group without a regular daytime activity differed from the other groups of daytime activity

by having higher frequencies of maladaptive behavior, anxiety, and depression, and the lowest level of QoL. The highest frequency of ID was found in the group engaged in customized education/occupation. Parental highest education was not associated with groups of daytime activity. However, ever having a part-time job, and availability and adequacy of support was associated with groups of daytime activity, as well as type of schooling and number of school changes during primary and lower secondary school. Importantly, different effects of these factors were found for the different groups of current daytime activity.

Overall, the results of this investigation illustrate the heterogeneity in outcomes for adolescents and adults diagnosed with ASD in childhood. The study population includes very well-functioning individuals, but also individuals more severely affected by behavioral problems, comorbidities, and low levels of adaptive functioning and QoL, in addition to apparent difficulties finding an appropriate daytime activity. However, compared with previously conducted follow-up studies on adolescents and adults diagnosed with ASD in childhood a more positive picture has emerged, with larger proportions doing well on the parameters investigated.

CHAPTER 7. PERSPECTIVES FOR FUTURE RESEARCH

On the basis of this project and the analyses conducted, there are several perspectives for future research involving further analyses using the existing dataset, as well as planning a future follow-up of the same cohort.

The dataset allows for further investigation of important issues of relevance to research in ASD. First, owing to the unequal sex distribution in ASD populations (e.g., Jensen et al., 2014) combined with the use of relatively small samples, investigations of potential sex differences have only been sparsely investigated (Howlin & Magiati, 2017). The role of sex is an important area in ASD research, which is not dealt with hugely in the present project. However, using the data collected, analyses of potential sex differences can be conducted. Second, adaptive functioning was analyzed very broadly in this project, using the GAC score only. Analysis on domain level of the ABAS-II may reveal important differences both for the total sample and across subgroups. Further, factors associated with adaptive functioning have not been thoroughly investigated. For example, the presence of ID will, to a high degree of certainty, be strongly associated with adaptive functioning, but whether contextual factors related to support and services, for example, are associated with adaptive functioning is unknown.

Additionally, new perspectives on data analysis can be applied. The psychometric properties of the INICO-FEAPS Scale could have been further investigated with item-response theory models. This approach has the advantage of taking into account each item in evaluation of a scale (Bortolotti, Tezza, Andrade, Bornia, & Sousa Júnior, 2013), and may have revealed results with implications for the use of the scale. Further, the results of the PhD project call for further investigations of the issues addressed, owing to the use of association-based statistical models applied with the aim of describing the study population. Hence, the variables investigated in this PhD project might be interrelated in different ways. Accordingly, it could extend and clarify the findings with application of analyses of mediation and interaction (dealt with in, e.g., Vanderweele, 2015). An important aim in performing such analyses is to try to understand the mechanisms through which a defined independent variable affect a certain outcome, and identify the role of each variable involved in the association between the independent variable and the outcome variable. For example, in this project an association was found between type of schooling and current daytime activity. However, other variables such as the presence of psychiatric comorbidity might impact on this association.

Last, a substantial group of responders – 80.5% of the parental responders and 81.5% of the responders with ASD – gave consent to be contacted for a future follow-up

study. Even though this project followed-up on adolescents and adults diagnosed with ASD in childhood, the assessments were one-point estimations comparable to cross-sectional studies. As stated by Kaboski et al. (2017), “ASD is remarkable for both its great heterogeneity in possible long-term outcomes and its tendency to vary over time in its manifestation of symptoms within an individual” (p. 177). Accordingly, longitudinal data on the study population will provide important information about the trajectories of these individuals, including clarifying information on factors improving the outcomes for individuals with ASD.

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ISSN (online): 2246-1302
ISBN (online): 978-87-7210-143-9

AALBORG UNIVERSITY PRESS